The Neonatal Abstinence Syndrome in Kentucky Annual Report is prepared by the Division of Maternal and Child Health, within the Kentucky Department for Public Health, under Commissioner Dr. Steven Stack. This report was made possible by the many individuals who contributed their time and efforts toward the prevention of NAS.

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Executive Summary

The Kentucky Public Health Neonatal Abstinence Syndrome (NAS) Reporting Registry received fewer reports of Neonatal Abstinence Syndrome (NAS) in 2019 than in 2015-2017, although the number increased from 2018. In 2019, there were 1,102 cases of babies with signs and symptoms of NAS; this accounts for 20.9 of every 1,000 live births among Kentucky residents. Rates are highest in Appalachian areas of the state, in some areas reaching 55 cases per 1,000 live births. In comparison, the most recent national estimate for NAS was 7.3 cases per 1,000 live births (HCUP Fast Stats, 2020). Mothers of infants with NAS tend to have less education, be unmarried, and have more children, which may suggest lower socioeconomic status, a lack of social support, or reduced access to services.

The most frequent opioids reported were buprenorphine (65%), heroin (22%), and methadone (11%). Other commonly used substances are amphetamines, including methamphetamine (32%) and cannabinoids (26%). All other substances were used by less than 12% of women in the registry. Approximately 65% of cases were exposed to more than one type of substance during pregnancy; for these cases, the average exposure was three substances.

Prenatal care is critical for these women to address substance misuse and other co-occurring problems, such as hepatitis C, which was reported in about 36% of this population. Compared to women whose infants do not have NAS, mothers of infants with NAS are more likely to utilize Women, Infants, and Children (WIC) services during pregnancy, but much less likely to receive first trimester prenatal care. Inadequate health insurance may explain part of this disparity, as nearly 17% of women did not have insurance of any type to pay for their delivery. Enrollment in and compliance with Medication for Opioid Use Disorder (MOUD) is one factor associated with adequate prenatal care. About 55% of the women in the registry were estimated to be enrolled in MOUD. Of these, 63% were using other drugs not compliant with their treatment.

Infants with NAS are twice as likely to have a low birth weight and three times as likely to be admitted to a neonatal intensive care unit. Tobacco use co-occurs with substance use at high rates, which could further affect the health and development of these infants. Infants with NAS had longer delivery hospitalizations: 13.4 days as compared to 3.8 days for infants without NAS. Infants who received pharmacological treatment (44%) had average stays of 19.5 days. Among this group, the most common treatment was morphine (89%), followed by clonidine (35%); about 37% received multiple medications.

About 85% of infants with NAS were referred to the Department for Community Based Services, and 76% of those cases were accepted for investigation. Data from other Kentucky programs indicates that NAS is a risk factor for fatal or near-fatal child abuse including abusive head trauma and Sudden Unexpected Infant Death (SUID).

In addressing NAS and the issues of families affected by substance use, the Kentucky Department for Public Health recommends: continuing to promote prenatal care; promoting enrollment in MOUD programs; implementing a plan of safe care including educating parents and medical/child care providers on safe sleep, abusive head trauma, child abuse and neglect; enrollment in services such as WIC and home visiting; and improving access to long-acting reversible contraception.
Background

The Opioid Epidemic

Opioid misuse is widespread and severe and, recently, it has been the focus of prevention efforts across the nation. Appalachia may be the area that is hardest-hit by the epidemic, with some of the highest opioid prescription rates in the United States (U.S.) (CDC, “U.S. County Prescribing Rates,” 2017). Many rural Appalachians believe that drug addiction and misuse is the biggest problem facing their communities (NPR, RWJF, Harvard, 2018).

Opioids are a class of narcotic substances that bind to receptors in the brain to produce pain relief, anesthesia, or euphoria (Hughes et al., 2016). Prolonged use causes tolerance, or the need for increasing doses to produce an effect, which can lead to non-fatal or fatal drug overdoses (ACOG, “Opioid,” 2017). Non-fatal overdoses can result in kidney failure, heart problems, nerve damage, and anoxic brain injuries (Clark, 2014).


Surveys by Foundation for a Healthy Kentucky found that two out of every three Kentuckians know someone who has experienced problems as a result of drug use, and more than twice as many people knew someone who used heroin in 2018 than in 2013 (2019). Reported methamphetamine use also increased during this time.

Impact on Maternal and Child Health

Infants with prenatal substance exposure, including opioid exposure, may experience Neonatal Abstinence Syndrome (NAS). NAS is the effects of discontinuing prenatal substance exposure (Kocherlakota, 2014). Many over the counter or prescription medications can cause NAS (Hudak & Tan, 2012), so the diagnosis does not inherently indicate illicit activity by the mother. NAS presents similarly to withdrawal in adults, including restlessness, tremors, seizure, vomiting, fever, sweating, and apnea (Hudak & Tan, 2012). Symptoms may vary in presentation, duration, and severity and some babies with prenatal substance exposure may not experience NAS at all. Because symptoms are non-specific, toxicology screenings and maternal history are important in establishing in utero exposure. NAS can be treated by comfort care such as swaddling, rocking, and reducing environmental stimuli (Kocherlakota, 2014), but pharmacological intervention is sometimes used in severe cases. Treatment for NAS may take place in a Neonatal Intensive Care Unit (NICU) or other special care units.

Between 1999 and 2014 in Kentucky, the rate of opioid use disorder (OUD) increased 48-fold to 19 cases per every 1,000 deliveries (Haigh, Ko, Tong, Bohm, & Callaghan, 2018). However, women with OUD make up only a fraction of the estimated one in fifteen who took opioids during pregnancy (Ko et al., 2020).
Methodology and Limitations

In 2013, the Kentucky General Assembly enacted Kentucky Revised Statute (KRS) 211.676, establishing NAS as a reportable disease. Mandatory statewide reporting to the Public Health NAS Reporting Registry (from here on, “the NAS Registry”) began on July 15, 2014. The NAS Registry collects information from Kentucky hospitals on Kentucky resident children with NAS and a history of prenatal substance exposure. Case reporting is not tied to the International Classification of Disease (ICD-9 or ICD-10) codes.

KRS 211.678 outlines the confidentiality requirements of the NAS Registry and calls for an annual report of aggregated data. This annual report includes the calendar year 2019 births. Cases were linked to the Certificate of Live Birth to obtain additional information and to provide a comparison group. Cases were excluded if they did not meet all criteria: Kentucky resident, born in 2019, with NAS symptoms. Duplicate cases were also excluded.

Unless otherwise stated, all figures and tables show preliminary unduplicated case counts of Kentucky residents for the birth year 2019 from the NAS Registry and the Office of Vital Statistics. Any category with less than five (<5) cases is suppressed, and categories with 5-19 cases should be interpreted with caution as rare outcomes may lead to unstable estimates. Results may be presented as rates of NAS per 1,000 live births, calculated as follows:

\[
\text{Number of cases} \times 1,000 \\
\text{Total number of live births}
\]

The NAS Registry is a passive surveillance system, and as such is limited by the reporting practices of different hospitals or individual hospital employees. Overall, 31 hospitals reported 2019 cases to the NAS Registry. Delayed reporting can negatively affect data quality. For 2019 cases, 53% were reported more than 30 days after birth; the average time to submission was 66 days. The data system does not differentiate the details of timing and intent of substance use, which affects data on polysubstance use and Medication for Opioid Use Disorder (MOUD). Finally, Kentucky resident births that occur at facilities outside of Kentucky and are not transferred to a Kentucky hospital are not reported to the NAS Registry, which could result in underreporting near state borders.
Data and Results

Kentucky Incidence

Kentucky’s NAS rate remains far above the national average. Data from the NAS Registry shows 1,102 unduplicated cases in 2019, which is an increase from 2018 (Figure 1).

There are large discrepancies within Area Development Districts (ADDs) across Kentucky with rates ranging from 1.3 to 55.7 cases per 1,000 live births (Figure 2). In Kentucky, the rate of NAS in rural counties is nearly twice the rate in urban counties, with the highest rates in Appalachia.

Figure 2. NAS Rate By ADD of Residence, 2019
Mothers of infants with NAS (compared to mothers of infants without NAS) tended to have less education, be unmarried, and have more children (Figure 3). Those factors may indicate lower socioeconomic status, less social support, lack of access to family planning services, or limited health literacy. Identifying demographic patterns and addressing social determinants of health are important steps in developing interventions to reach high-risk populations.

Figure 3. Education, Marital Status, and Pregnancies of Mothers by NAS Status of Child, 2019

Frequent Substances Used

Table 1 includes all substances included in the NAS Registry (excluding tobacco and alcohol) by category, ranked from most to least commonly reported. This table takes into account any indication of exposure (maternal history, maternal toxicology screen positive, and/or infant toxicology screen positive). From year to year, there have been no major changes in the rankings of substances.

Table 1. Frequency of All Substance Groups in the Public Health NAS Reporting Registry, 2019

<table>
<thead>
<tr>
<th>Frequency of Opioids in the Public Health NAS Reporting Registry</th>
<th>Frequency of Other Substances in the Public Health NAS Reporting Registry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any of the below opioids 88.66%</td>
<td>(Meth)Amphetamines 32.21%</td>
</tr>
<tr>
<td>Buprenorphine 64.97%</td>
<td>Cannabinoid 26.13%</td>
</tr>
<tr>
<td>Heroin 21.51%</td>
<td>Benzodiazepines 11.89%</td>
</tr>
<tr>
<td>Methadone 10.53%</td>
<td>Cocaine 7.80%</td>
</tr>
<tr>
<td>Oxycodone 8.98%</td>
<td>Gabapentin 5.35%</td>
</tr>
<tr>
<td>Fentanyl 7.26%</td>
<td>SSRIs 3.09%</td>
</tr>
<tr>
<td>Hydrocodone 3.81%</td>
<td>Barbiturates 1.36%</td>
</tr>
<tr>
<td>Tramadol 0.73%</td>
<td>Tricyclics 1.09%</td>
</tr>
<tr>
<td>Naltrexone 0.09%</td>
<td></td>
</tr>
<tr>
<td>Unspecified Opioids 28.58%</td>
<td></td>
</tr>
</tbody>
</table>

Note: Numbers will not add to 100% as more than one substance can be reported per case and not all substances are shown in the table above. The category (Meth)Amphetamines includes any indication of use of methamphetamine and/or amphetamines.
The most common substance in the NAS Registry is buprenorphine, a partial opioid agonist with low potential for abuse which is used to reduce withdrawal and cravings (SAMHSA, 2016). While it can be associated with NAS, its use as part of supervised MOUD is preferable to untreated OUD during pregnancy. Increased access to MOUD may explain why buprenorphine is one of the most common substances in the NAS Registry every year. The second most common reported substance was “all other opioids,” which were reported about two out of every five cases. Non-specific toxicology reports or maternal histories of opioid use make up the majority of this category. Fentanyl use, although still rarely reported in the NAS Registry, nearly doubled from 2018 to 2019 (3.86% to 7.29%).

The reported frequency of amphetamine use, including methamphetamine, has been increasing in recent years; in 2017, it was reported in only 23.07% of cases, compared to 32.21% in 2019.

More than one-quarter of the cases in the NAS Registry were exposed to cannabinoids. Cannabis is the most commonly used illicit drug in the U.S., with about 7%-15% of pregnant women likely using it (McCance-Katz, 2018; Garg et al., 2016). Women who use cannabis during pregnancy believe there are few adverse effects compared to the perceived therapeutic value (Weisbeck et al., 2020). The American College of Obstetricians and Gynecologists (ACOG) discourages marijuana use during pregnancy due to a lack of studies on its safety (ACOG, “Marijuana,” 2017). Although cannabis is not known to cause NAS, it is associated with pregnant women using other substances, including tobacco, alcohol, and opioids (Passey, Sanson-Fisher, D’Este, & Stirling, 2014).

About 65% of cases had polysubstance use, which in this report means the use of substances from more than one type or category (see Table 1), excluding tobacco and alcohol. About 32% of women used two types of substances, and about 33% used three or more types of substances; on average, cases with polysubstance use had exposures to three types of substances. Polysubstance use may contribute to prolonged or more severe NAS symptoms. Substances such as cocaine, benzodiazepines (Hudak & Tan, 2012), and antidepressants (Kaltenbach et al., 2012) can be associated with worsened NAS symptoms when combined with opiates.

Over half (54.5%) of the women had a prescription for medications to treat addiction, indicating enrollment in MOUD. Prescriptions for pain treatment and psychiatric treatment were much less common (6% of women for each), which aligns with the low reported frequencies of those medications.

**Prenatal Care**

The prenatal period presents a unique window of opportunity for women to make many changes in their health and lifestyle, including management of OUD (ACOG, “Opioid,” 2017). About three out of every five mothers in the NAS Registry received at least adequate prenatal care (Kotelchuck index), compared to four out of five mothers who did not have infants with NAS.
As part of prenatal care, ACOG recommends women with OUD are screened for infections including hepatitis C (ACOG, “Opioid,” 2017). The Hepatitis C rate among mothers whose children did not have NAS was 1.7%, compared to 36.4% among those whose children had NAS. Among women with polysubstance use, it was 40.1%. These concerns led to the passage of Senate Bill 250 in April 2018, which added universal screening of pregnant women for hepatitis C to KRS 214.160.

Over half of the mothers whose infants had NAS received services through the Women, Infants, and Children program (WIC) during pregnancy. Enrollment in WIC can ensure proper nutrition for an infant who is at risk of feeding difficulties, provide assistance with breastfeeding, and refer mothers to additional services.

Disparities in insurance coverage, shown in Figure 5, give one possible explanation for disparities in prenatal care utilization. Four times as many deliveries of infants with NAS were paid out of pocket as opposed to deliveries of infants without NAS (16.6% versus 3.7%), and these mothers may lack insurance to cover prenatal care. With three-quarters of babies with NAS having Medicaid, as opposed to about half of the non-NAS population, Medicaid organizations have the ability to reach this population and work with them to promote prenatal, postpartum, and pediatric care. By ensuring appropriate preventive services, it may be possible to avoid costly outcomes in the future.

Another factor in prenatal care utilization is enrollment in and compliance with MOUD. Enrollment in both prenatal care and MOUD may provide additional benefits to mothers. MOUD uses counseling and mental health therapy approaches in addition to medications such as buprenorphine, methadone, or naltrexone.

In this report, MOUD means having a valid prescription for replacement therapy. Non-compliance is defined as concurrent use of meth/amphetamines, barbiturates, cannabinoids, cocaine, heroin, or any other opioid. These are proxy measures, as the NAS Registry does not collect compliance with MOUD. In the 2019 cohort, over half of the mothers were in MOUD but less than two-fifths of those were compliant (Figure 6). The low rate of compliance among mothers in MOUD parallels the high frequency of polysubstance use among the entire sample of cases in the NAS Registry. Although the rate of MOUD enrollment (55%) is similar to last year, the rate of compliance decreased by 16% (44% to 37%).
Newborn Outcomes

In the wake of the opioid epidemic, alcohol and tobacco are often overlooked although both forms of prenatal substance exposure can have negative effects such as developmental delays and preterm birth (Bishop et al., 2017) and can cause withdrawal-like symptoms in infants (Hudak & Tan, 2012). Kentucky Office of Vital Statistics data show that 14% of women whose babies did not have NAS reported smoking during pregnancy, which increases to 61% for women whose babies have NAS. Data collected in the NAS Registry is even higher with 77% of women reporting tobacco use. The prevalence of alcohol use during pregnancy is not well known, as it is vastly under-reported but is estimated to be approximately 10% (CDC, 2015). Alcohol use was reported by mothers of 4.6% of infants with NAS in Kentucky. Although under-reporting is still a concern, the NAS Registry provides a source of information on this topic.

Compared to infants without NAS, infants with NAS are nearly twice as likely to be low birth weight (LBW) defined as less than 2,500 grams. Underlying social, behavioral, and biomedical factors (Schempf & Strobino, 2008) may be partly responsible for this finding. Infants with NAS can have difficulties feeding and gaining weight (Hudak & Tan, 2012), which further increases the health risks and challenges associated with preterm and LBW.

These conditions are associated with medical complications that result in longer duration of hospitalization. In 2019, about one in ten newborns without NAS had NICU stays, compared to one in three newborns with NAS, and there is a national trend of NICUs dedicating increasing resources to NAS (Tolia et al., 2015). Infants with NAS also have a much longer length of stay (LOS): 13.38 days versus 3.76 days.

Figure 7. Length of Stay by NAS Status, 2019
As symptoms do not develop immediately (Kocherlakota, 2014), the American Academy of Pediatrics (AAP) (Hudak & Tan, 2012), and the World Health Organization (2014) both recommend observing infants with NAS in the hospital for four to seven days post-delivery. In 2019, the average age at onset of symptoms was 30.2 hours; 17% of cases in the registry did not develop symptoms until at least 48 hours after birth.

One factor contributing to the length of stay is pharmacological treatment for NAS; infants receiving medication for NAS have a longer LOS than those who receive comfort care only (19.5 days compared to 6.1 days). Overall, 44% of infants with NAS received one or more medications to treat NAS. Nearly nine out of every ten treated infants received morphine, which is consistent with research on prescribing practices (Hudak & Tan, 2012). Clonidine was used in over one-third of treated cases, although there are few studies on its use to alleviate NAS symptoms in infants (Hudak & Tan, 2012). All other medications were administered to <15% of infants who received medication. Over one-third of infants who received treatment were prescribed more than one medication. When considering pharmacological treatments for NAS, the first concern is that treatment should be both safe and effective. NAS may cause distress or discomfort but it is ultimately self-limiting, and unnecessary medication may prolong or exacerbate the process (Hudak & Tan, 2012).

Some interventions that help reduce the severity of NAS can be provided instead of or in addition to pharmacological treatment. Breastfeeding may reduce the severity of NAS symptoms (Hudak & Tan 2012; ACOG, “Opioid,” 2017). From birth certificate data, mothers of infants with NAS are much less likely to plan to breastfeed as mothers of infants without NAS (39% vs 73%, respectively); according to the NAS Registry, only about 21% initiate breastfeeding.

**Outcomes Beyond Discharge**

In addition to the lack of insurance, women with OUD might have less interaction with the healthcare system because they fear civil or criminal charges or reporting to child welfare agencies. These fears are not baseless, as many states define substance use during pregnancy as child abuse (Guttmacher Institute, 2019). As part of the
Child Abuse Prevention and Treatment Act (CAPTA), states must have policies to notify child welfare agencies about infants with prenatal substance exposure. Nationwide, in fiscal year 2019, over 86,000 children entering foster care had parental drug abuse as a circumstance of removal from the home (Children’s Bureau, 2020).

As stated in the Kentucky Cabinet for Health and Family Services (CHFS) Department for Community Based Services, Division of Protection and Permanency standard of practice manual, reports may be accepted alleging risk of harm if a “caretaker engages in a pattern of conduct that renders him/her incapable of caring for the immediate and ongoing needs of the child” due to substance misuse (2020). That policy includes the example of infants testing positive or experiencing withdrawal from non-prescribed substances. For that reason, medical providers are expected to document prenatal substance exposure in the medical record. Of all infants in the NAS Registry, 85% were referred to DCBS; 76% of those were accepted. The referral rate is very similar to what was reported last year, indicating consistency of practice; the acceptance rate decreased from last year’s 81%. Among infants whose mothers were estimated to be compliant with MOUD, 81% were referred to DCBS and 49% of those were accepted for investigation.

The Child Fatality and Near Fatality External Review Panel (“the Panel”) conducts comprehensive, multidisciplinary reviews to discover risk factors and systems issues and recommend prevention measures (2019). Historically, a large proportion of cases, especially abusive head trauma cases, have had caregiver substance misuse as a risk factor. Recommendations from the Panel have been incorporated into this report.

Data from Kentucky’s Sudden Unexpected Infant Death (SUID) Case Registry shows that in 2016-2018, 29% of cases had a risk factor related to substance use (including NAS and parental/caregiver use). This data could indicate that NAS is a risk factor for SUID, but there is not a known biological mechanism for that relationship. Caregiving or co-sleeping while impaired could also endanger infants.

**Concluding Statement**

NAS is just one facet of the opioid epidemic and cannot be addressed in isolation from larger systemic issues. Although the problem is daunting, prevention is possible. The following recommendations help address the underlying determinants of health to promote better outcomes for families and children.
Recommendations for Prevention

Promote optimal periconceptual health and prenatal care. Optimal periconceptual status promotes healthy pregnancy. Prenatal care ensures monitoring for any medical or fetal complication and screening for substance use disorder and co-morbidities so that referral can be made for treatment and counseling.

Referral and enrollment in MOUD programs. In the NAS Registry over half of the women report having a prescription for replacement therapy. MOUD programs, especially those that incorporate comprehensive services to address the complex needs of the mother and family, can be very successful in addressing OUD. To support recovery, MOUD should be more accessible for both pregnant and postpartum women. Furthermore, all MOUD providers need training in family-oriented protocols for counseling and behavioral therapy, which are crucial to the success of treatment programs. Regulatory authorities should require MOUD providers to participate in collaborative and holistic services directed to pregnant women, or mothers and their infants.

Implement a plan of safe care. Every infant, including those prenatally exposed to drugs or alcohol, should leave the hospital with an appropriate plan of safe care. A plan of safe care should address coordinated and integrated services needed for the impacted child, parent(s), and caregivers. The Kentucky Department for Public Health (KDPH) has the community outreach structure in place to help bridge the widening gap between the need for and availability of services or resources. Interagency collaboration among the Department for Behavioral Health, Developmental and Intellectual Disabilities, Department of Community Based Services, and KDPH will assure that plans of safe care are implemented for infants with NAS or any substance exposure.

Education for parents on abusive head trauma and safe sleep. Birthing hospitals provide in-person, evidence-informed education regarding safe sleep and abusive head trauma prevention to parents, both antepartum and postpartum. Continuing this as universal practice will ensure that all parents of infants with NAS or prenatal substance exposure are reached. To that end, the Kentucky Hospital Association supports this practice. The KDPH continues to promote the ABCD of safe sleep practice (Babies sleep Alone, on their Back, in a Crib, and attended to without Danger from a caretaker who is impaired, tired, or distracted).

Implement the practice of modeling safe sleep among healthcare and childcare providers. Infants with NAS have an increased risk of SUID, which may be reduced through safe sleep practices. Healthcare and childcare providers are uniquely positioned to encourage these practices through modeling and should do so universally.

Increase enrollment in services such as WIC and HANDS. Programs that serve mothers and families prenatally and throughout early childhood have unique opportunities for engagement. These programs should incorporate substance use disorder education into curricula on healthy pregnancies, in addition to making referrals to counseling or treatment, community resources, and monitor the parent’s and child’s well-being. For more information, families can visit http://www.kyhands.com/.

Improve access to long-acting reversible contraception (LARC). Only 16% of infants with NAS were the first live birth to that mother, compared to 37% of infants without NAS. This demographic trend has been consistent across the past few years, with the additional context that nearly 90% of pregnancies among this population are unintended (Heil et al., 2010). This trend could indicate a need for more effective pre-conception counseling, including improved access to family planning among women of reproductive age who use opioids for any purpose. Kentucky Medicaid covers LARCs, and other insurers and providers should work to make LARCs accessible to all interested mothers during the intrapartum period.
References


Kentucky Cabinet for Health and Family Services (CHFS) Department for Community Based Services, Division of Protection and Permanency (2020) Standard of Practice Manual 2.3 - Acceptance Criteria and Reports That


