ARTICLE

Neonatal abstinence syndrome: Effectiveness of targeted umbilical cord drug screening

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OBJECTIVE: This study sought to determine if targeted drug screening of newborns was effective in identifying a positive drug test result.
STUDY DESIGN: This was a retrospective cross-sectional study. A total of 340 infants met criteria for drug screening. Sensitivity and specificity were used to evaluate each of the potential risk factors in terms of their ability to predict a positive drug test result. Two-sample t-tests were used to compare differences in Finnegan scores between babies with a positive drug test result and those with a negative one.
RESULT: The risk factor with the highest sensitivity was maternal history of drug use. The difference in the Finnegan scores between groups was statistically significant.
CONCLUSION: The risk factors associated with this study were not very sensitive. The only way to identify all infants at risk of NAS is to standardize the screening process and apply to all infants.

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INTRODUCTION

Neonatal Abstinence Syndrome (NAS) is a growing health problem in the United States. From 2004 to 2018, the incidence of NAS in the United States increased from 1.5 per 1000 hospital births to 6.8 per 1000 hospital births, a more than 350% increase [1, 2]. NAS is a condition in which an infant experiences withdrawal from uterine exposure to various substances such as oxycodone, heroin, buprenorphine, and morphine. Although most withdrawal assessment tools were developed for infant's exposed to opioids, some researchers also consider non-opioid substance exposure when defining NAS. Depending on the severity of the symptoms, these infants may experience a longer hospital stay and may require treatment and monitoring in the neonatal intensive care unit (NICU), resulting in an increase in healthcare costs. NAS can lead to withdrawal symptoms within the first few days of life that include central nervous system (CNS) disturbances, vasomotor dysregulation, gastrointestinal disturbances, and hyperirritability such as tremors, fever, tachypnea, excoriation, diaphoresis, high-pitched crying, lack of sleep, vomiting, diarrhea, and more severe symptoms such as seizures and respiratory distress [3–5]. While more research is needed in the area, a preliminary finding is that infants with NAS in the neonatal period have also been shown to be at increased risk of long-term problems with their vision, behavior, cognition, sleep, and hearing [6].

Determination of risk for NAS can be evaluated in a number of ways in regard to drug screening mothers and/or infants [7]. Drug testing can be performed on maternal or infant blood, urine, or hair as well as infant meconium, umbilical cord, or placenta [4, 8]. Screening can be targeted, where drug testing is performed only if certain criteria are met. The goal of targeted drug screening of newborns is to identify newborns at risk for NAS by using risk factors often associated with maternal substance use. Drug screening can also be universal, where all mothers or infants are chosen for drug testing. Early identification of infants at greatest risk for NAS can help determine infants who would benefit from early intervention and monitoring. The objective of this study was to determine if targeted drug screening of newborns is effective in identifying a positive drug test result. This study sought to compare drug testing results to the associated selective drug screening criteria to determine which screening criteria were most sensitive to confirmed substance exposure. In addition, Finnegan scores were compared between infants with positive drug testing results and those with negative drug testing results to evaluate whether there was a significant difference in the highest and average recorded scores between these groups.

METHODS

Design and sample

This study was a retrospective cross-sectional medical record review that involved collecting data on all infants born between September 1st, 2015 and September 1st, 2016 who met criteria for umbilical cord drug screening based on targeted screening criteria ($N = 340$; see Table 1). These targeted screening criteria were not manipulated or chosen for the purpose of this research. The targeted screening criteria were already being utilized at this facility and the research was conducted retrospectively to measure effectiveness. Infants born prior to September 1st, 2015 and after September 1st, 2016, and those infants that did not meet umbilical cord drug screening criteria were excluded from this study (see

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Table 1. Frequency distributions for all targeted drug screening criteria specific to the institution chosen for this study ($N = 340$).

Targeted Drug Screening Criteria	Frequency	Percent (%)	Sensitivity	Specificity
History of drug use	113	33.2	51.9	72.7
Minimal prenatal care	48	14.1	14.3	85.9
Late prenatal care	42	12.4	13.0	87.8
No prenatal care	4	1.2	2.6	99.2
Precipitous labor	32	9.4	10.4	90.8
Severe mood swings	2	0.6	1.3	97.0
Unexplained sores on skin	7	2.1	0	97.3
Abruptio placentae	9	2.6	1.3	97.0
Inappropriate behavior	17	5.0	2.6	94.3
Myocardial Infarction in mother	0	0	0	100.0
Poor dentition	36	10.6	10.4	89.4
Unexplained fetal demise	0	0	0	100.0
Cerebrovascular accident in mother	0	0	0	100.0
Repeated spontaneous abortions	23	6.8	5.2	92.8
Unexplained severe hypertension	0	0	0	100.0
Myocardial infarction in healthy term newborn	0	0	0	100.0
Urogenital anomalies	1	0.3	0	99.6
Abnormal neuro behaviors	11	3.2	1.3	96.2
Necrotizing enterocolitis in healthy term newborn	0	0	0	100.0
Cerebrovascular accident in healthy term newborn	0	0	0.0	100.0
Unexplained intrauterine growth restriction	7	2.1	1.3	97.7
Preterm less than 36 weeks	4	1.2	0	98.5
Pediatrician (MD) Order	16	4.7	0	93.9

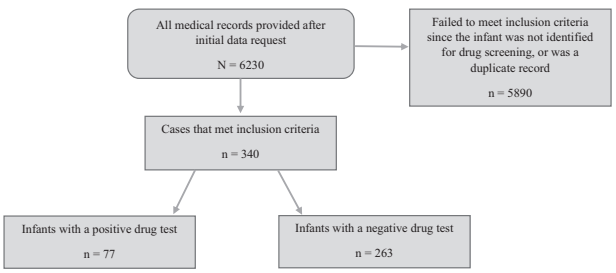

Fig. 1 Initial data request resulted in 6230 medical record numbers ($N = 6230$). The medical record numbers were then reviewed and all duplicates were eliminated, as well as those medical record numbers that did not meet the inclusion criteria ($n = 5890$). The remaining medical record numbers made up the final sample size ($n = 340$). These were then divided based on the final drug test results ($n = 77$ for positive, $n = 263$ for negative).

Fig. 1). An IRB application was submitted to the University of Kentucky's and Baptist Health Lexington's IRBs and both were approved in September 2019, including a waiver of informed consent. Although two IRB applications were submitted and approved, only one hospital was utilized for this research.

Measures

Data for this study was accessed using the electronic health record (EHR). Variables extracted from the EHR included demographics (gender, race/ethnicity, age of mother, and gestation at birth), admission, assessment, and discharge information (need for NICU admission for NAS treatment with morphine therapy, average Finnegan score, highest Finnegan score, and length of stay), and outcomes (individual targeted screening criteria met for mother, individual targeted screening met for infant, and the result of the drug screen).

Drug screening at this facility involved assessing mothers and infants for specific criteria (see Table 1) that would suggest the possibility of a positive drug testing result. If the mother and/or infant met at least one these criteria, a 6–8 inch piece of the umbilical cord was sent for drug testing to the United Stated Drug Testing Laboratories, Inc. (USDTL). The panel name for the test was Umbilical Cord Testing, the panel description was Umbilical Cord Testing Drug Panel, and the type was Profile [9]. Umbilical cord samples were saved from all deliveries, but were only sent for testing if at least one of these specific criteria were met. Negative results were usually available within one business day of sending the umbilical cord, while positive results were available after an additional 1–2 business days while confirmatory testing was being performed. Confirmatory testing consisted of using a second portion of the umbilical cord for testing to alleviate frame shift errors [10]. If the confirmation results were different from the initial result, this alerted the laboratory to the possibility of a frame shift error and an investigation was begun. The initial drug test was a sensitive and quicker immunoassay test used to separate the negative results. The confirmation test utilized slower gas chromatography/mass spectrometry, gas chromatography/tandem mass spectrometry (GCMS, GCMSMS) or liquid chromatography/tandem mass spectrometry (LCMS). Jones [10] stated that these confirmatory testing techniques are the gold standard for confirming drugs of abuse in biological samples. While awaiting the results of the drug screening, any infant who had an umbilical cord sample sent would be assessed for withdrawal using the Finnegan scoring tool. Without maternal risk factors present to trigger sending the umbilical cord for testing immediately after birth, neonatal risk factors often presented within the first 24–72 h of life and the umbilical cord was sent for testing once neonatal risk factors were identified. Infants were scored every 4 h once criteria was met for drug screening, and if an infant was found to have three consecutive scores of 8 or more or two consecutive scores of 12 or more, they were admitted to the NICU for further monitoring and pharmacological treatment. Finnegan scoring was recorded until the infant was discharged or until the results of the drug testing were available. If an infant was found to be positive for a substance other than an opioid, Finnegan scoring was stopped.

Data analysis

Sensitivity and specificity were used to evaluate each of the potential risk factors in terms of their ability to predict a positive drug test result. Two-sample *t*-tests were used to evaluate differences in average and highest Finnegan scores between babies with a positive drug test result and those

Table 2. Group comparisons of Finnegan scores between neonates with a positive and negative drug screen results ($N = 340$).

	Mean	Standard Deviation	|t|	*p*
Average Finnegan Score				
Negative Drug Test ($n = 263$)	1.1	1.3	2.0	0.05
Positive Drug Test ($n = 77$)	1.5	1.7		
Highest Finnegan Score				
Negative Drug Test ($n = 263$)	3.2	2.9	2.6	0.01
Positive Drug Test ($n = 77$)	4.5	3.9		

with a negative test result. Data analysis was done using SPSS, v. 26; an alpha level of 0.05 was used.

RESULTS

For the 340 infants included in the study, the average maternal age was 26.0 years old (SD = 5.7) and the average gestation at birth was 38.1 weeks (SD = 2.6). The mean for the average Finnegan score was 1.2 (SD = 1.4) and the mean for the highest Finnegan score was 3.5 (SD = 3.2). The average length of stay for infants was 3.8 days (SD = 5.6). With this average being affected by the relatively large number of days some infants were hospitalized in the NICU, the median was used to assess the number of days most infants were in the hospital, since this measure is not affected by outliers. This showed that more than half of infants were hospitalized for 2 days or fewer. If an infant was preterm or required morphine therapy in the NICU, the length of stay ranged as high as 50 days.

Within the sample, slightly more than half of neonates were female (52.0%), and the majority were Caucasian (78.0%). Of the 340 infants in the sample, seven (2.1%) required morphine therapy for withdrawal treatment and were admitted to the NICU. When treating infants with morphine in the NICU for high Finnegan scores, the infant or mother must have tested positive for opiates. Out of the 340 umbilical cord samples, 40 (11.7%) were positive for opiates. Of those infants that were positive for opiates, 17.5% required treatment with morphine.

A total of 77 (22.6%) infants tested positive for the following substances: amphetamines (1.5%), cocaine (0.9%), opiates (11.7%), cannabinoids (9.7%), methadone (0.9%), and benzodiazepines (0.3%). The maternal and infant risk factors used to drug screen all infants at this facility showed 113 (33.2%) mothers had a history of drug use (Table 1). Infant risk factors were listed as criteria in 8.8% of those who were tested.

The risk factor with the highest sensitivity was maternal history of drug use, with a sensitivity of 0.519 (specificity 0.727) (Table 1). Minimal prenatal care had a sensitivity of 0.143 (specificity 0.859), late prenatal care 0.130 (specificity 0.878), precipitous labor 0.104 (specificity 0.908), poor dentition 0.104 (specificity 0.894), and the remaining risk factors had sensitivities of less than 0.100. Based on the two-sample t-tests, the difference in the average Finnegan scores and highest Finnegan scores for those infants with a positive drug test result compared to those infants with a negative drug test result was statistically significant (Table 2).

DISCUSSION

In using these data to identify whether risk factors were effective in identifying a positive drug test result, none of the risk factors were very sensitive. The results of this study showed that the targeted screening criteria utilized at this facility were not the best predictors of a positive drug test and, therefore, did not serve as reliable criteria in which to send umbilical cord samples for drug testing or to assess those infants for withdrawal. With the rise in NAS and the need to properly assess infants for withdrawal, a more reliable screening protocol is needed.

A larger percentage of hospitals performed targeted screening as opposed to universal screening when reviewing the literature. Bogen et al. [11] found that 90% of 76 hospitals from 34 states used risk-based screening compared to 3% that used universal screening. Miller et al. [12] found that among 31 Maryland hospitals, 48% used targeted screening compared to 45% who used universal screening. Wood et al. [13] found that in 69 Iowa hospitals, 90% used targeted screening and 0% used universal screening. Studies describing maternal risk factors associated with targeted drug screening included a variety of criteria, and chosen risk factors were not standardized across facilities. Examples of risk factors among multiple studies included a positive history of maternal drug testing at delivery or during pregnancy, a history of substance use disorder before pregnancy, limited or no prenatal care, maternal legal involvement, prior Child Protective Services (CPS) involvement, other offspring not in custody, placental abruption, preterm labor, maternal tobacco or alcohol use, HIV positive status, HbsAg positive status, Hepatitis C positive status, history of gonorrhea or syphilis, fetal demise, precipitous delivery, intra-uterine growth restriction (IUGR), unintended delivery outside of the hospital, and acting intoxicated during office visits or on admission to the hospital [11, 12, 14–20].

Although screening by risk factors can reduce cost, bias has been found to exist in how providers determine who should be screened and who they report to social services. In a study described by Terplan and Minkoff [7], black women and poor women were more likely than others to be reported to social services, and infants of black women were more likely to be drug screened. Another study by Ellsworth et al. [16] identified 565 mothers that met criteria for targeted screening protocols, but only 20.7% of these women were actually screened. Of those screened appropriately, infants born to black mothers were three times more likely to be screened compared to white mothers. In assessing infants of mothers who did not meet any criteria for screening, infants of black mothers were four times more likely to be screened not having any risk factors.

Researchers found that maternal drug testing not only revealed substance use during pregnancy, but showed women were not always honest in their self-reports of substance use due to fear of discrimination and legal retribution. Risk factors alone did not always determine whether a woman would have a positive drug test result and risk factors can vary greatly among facilities. When studying the prevalence of substance use by pregnant women in the office setting, Kreshak et al. [21] and Schauberger et al. [22] found that 13–30% of women tested positive for one or more substances in urine samples. Of those samples found to be positive, marijuana and opioids had the highest prevalence. Three studies examined the difference in maternal self-reports and risk factors in comparison to universal infant drug screening results [17, 19, 22]. Lange et al. [23] found that detection of alcohol in meconium samples was four times higher than what was admitted in maternal self-reports, Murphy-Oikonen et al. [17] found that mothers failed to admit drug use in 27% of positive urine samples and 24% of positive meconium samples, and Wexelblatt et al. [19] found that 20% of opioid-positive urine drug screenings of infants occurred in mothers without standard risk factors.

This study utilized umbilical cord drug screening as the tool for detection of maternal substance use. Prior to umbilical cord drug testing, meconium was the most common material tested on infants [24]. Although effective, meconium testing has limitations including passage of meconium prior to delivery, delayed meconium passage after delivery, insufficient quantity, and difficulty collecting samples due to multiple collectors needing to be involved. Umbilical cord testing and meconium testing both have a window of detection of up to 20 weeks before delivery [25]. Urine has many of the same limitations as meconium and only shows a history of the last 2–3 days. Hair is often difficult to test due to the limited amount of hair available on newborns as well as the need to shave parts of the head to obtain sufficient quantities [24]. Hair has a detection window of up to 3 months. In umbilical cord tissue, substances are distributed uniformly compared to non-uniform distribution in meconium [24]. This means that the entire amount of meconium in an infant must be obtained and sent for testing in order for the maximum amount of drug(s) to be detected [25]. Studies found that umbilical cord and meconium testing did not differ significantly in rates of drug detection, and umbilical cord testing was better because it decreased missed collections, increased detection of iatrogenic medications provided during labor, decreased tampering of the sample, and eliminated insufficient sample volume [24].

Another comparison in this study considered differences in Finnegan scores between infants with positive drug testing results to infants with negative drug testing results. The Finnegan scoring tool is the most commonly used scoring system for evaluating infants with NAS [26]. Developed in 1975, it consists of 21 scored items or symptoms involving the central nervous system, the autonomic nervous system, and the gastrointestinal system. Higher scores are consistent with NAS. The recommendation for practice with the Finnegan scoring tool is to consider further monitoring and initiation of pharmacological treatment if the infant has three consecutive scores of eight or more or two consecutive scores of 12 or more [26]. While performing the medical record review, it was noted that many infants with negative drug testing results had high Finnegan scores. This could have been due to the infant withdrawing from other substances not tested on the 9-panel drug screen that was ordered, or it may have been due to the subjective nature of the Finnegan scoring tool and the difference in the nurses who scored the infants throughout the hospitalization. In performing a two-sample t-test on the average Finnegan scores and the highest Finnegan scores, it was found that the average and highest Finnegan scores were significantly higher for the positive result group compared to the negative result group. This suggests that, on average, there is a significant association between Finnegan scoring and drug testing results, even though some in the negative group had relatively high scores and some in the positive group had relatively low ones.

One limitation of this study was the relatively small sample size given the low prevalence of some risk factors. Some risk criteria were not found in any of the infants or their mothers; a larger sample size would allow a better quantification of the sensitivity and specificity of each risk factor. In addition, not all applicable risk factors were noted in the medical records of each infant. If a drug screening was performed after the infant was born, the reason for doing so was often not included in the EHR. It was also unknown if an infant only had one risk factor recorded because that was all that was required to trigger a drug screen or if the infant truly only had one risk factor present. Another limitation in this study was that the criteria for screening chosen by the facility where this research took place was not all inclusive of the risk factors found in the literature review. By studying all possible risk factors, more data could be obtained to find those with the best sensitivity and specificity. During the time frame chosen within the inclusion criteria, the hospital in this study utilized a 9-panel umbilical cord drug screen which included Amphetamines, Cannabinoids, Cocaine, Opiates, Phencyclidine, Methadone, Barbiturates, Benzodiazepines, and Propoxyphene. With there now being a 17-panel umbilical cord drug screen, there may have been additional substances missed given that they were not included in the panel used for this study. Although the same infants would have been tested based on the positive risk factors, this might have resulted in more positive drug screenings among those identified as at risk. An additional limitation is that some maternal factors (including gravida, parity, and socioeconomic status) were not available in the retrospective data collection. Had they been available, this information would have provided more context to our findings.

One of the greatest limitations of this study was the inability to know drug testing results for infants who were not identified as at risk due to maternal or infant characteristics, as these infants were not tested. It would have been ideal to have completed screening information and drug testing for all infants born during the identified time period, but this would have been cost prohibitive. The cost of a 13-panel umbilical cord drug test (which was the newest panel being ordered by the facility used for this study) was $177.00 and was paid by the hospital. With a hospital average of 1600 live births a year at this facility, this would have resulted in over 1200 additional umbilical cord drug tests. The increase in this cost would have been over $220,000. Without the resources to test all infants, there is not a complete view of the sensitivity and specificity of these risk factors as they relate to a positive drug screen. Still, the poor sensitivity of nearly all risk factors underscores that these criteria are relatively futile in identifying uterine drug exposure, especially since there is no standardization to the risk factors across facilities. This suggests that broader testing criteria are needed to ensure exposure is identified early.

CONCLUSION

The main goal of this research was to determine if risk-based screening was efficient in determining a positive drug test result. Based on the statistical analysis, the risk factors associated with this study were not sensitive in discovering positive umbilical cord drug test results. Maternal history of drug use was the only risk factor that had a high enough sensitivity to suggest significance, and the sensitivity was only 0.519. Studies show that risk factors for drug screening vary across facilities and there are no specific guidelines for drug screening in pregnancy [11, 12, 14–20]. Given the subjective nature of many of the risk factors as well as the difference in risk factors across facilities, it was not surprising that most of the risk factors evaluated at this hospital were not effective in identifying a positive drug test. Measuring the sensitivity and specificity of other risk factors that are utilized by other facilities could help in standardizing the process of risk based screening. By utilizing the risk factors with the highest sensitivities, facilities can exclude those which are only chosen based on personal assumptions or biases, and screening can be more objective.

Some facilities have begun to universally drug test all mothers and/or infants routinely to avoid bias and allow simplicity [7]. As this research has shown, criteria for risk-based screening can be non-specific and subjective. With the rise in NAS and the severe symptoms that can result due to opiate withdrawal in infants, proper screening is necessary to identify those who are at greatest risk. This would be best accomplished by determining which criteria are the most sensitive and specific or by performing universal drug screening so that every infant has the opportunity to be tested.

The American College of Obstetricians and Gynecologists' (ACOG) [3] recommends universal screening as an essential part of obstetric care in order to improve maternal and infant outcomes. According to this committee opinion, screening in pregnancy may include validated verbal screening tools such as

questionnaires or may also include urine toxicology screening [3]. Risk based screening has high potential for bias, while universal screening can de-stigmatize the process of testing [8]. Substance use disorder during pregnancy is an important public health issue, but has many social, legal, and ethical implications when considering how to screen women and/or infants. Studies show that substance use during pregnancy is highly underreported due to fear of stigma and consequences [8, 23]. These mothers are at high risk of losing custody of their infants and many states consider substance use in pregnancy to be child abuse, which is why universal screening is often not supported [8, 23]. This can lead to pregnant women with substance use disorder avoiding prenatal care and treatment programs.

When considering the moral and ethical dilemma associated with universal drug testing of women and/or children, the move towards universal testing of pregnant women for HIV, Hepatitis B virus (HBV), and Hepatitis C virus (HCV) over the years involved similar concerns. Risk based screening was found to be ineffective at discovering all cases of HIV, HBV, and HCV in pregnant women, and rising numbers of cases in the Unites States made it an important health topic to address in order to improve health outcomes and reduce future pediatric treatment costs [27, 28]. It was found that risk-based screening resulted in missed cases and that providers often did not have the time or training to appropriately screen women effectively [27, 28]. Universal screening was also recommended due to improved treatment compliance during pregnancy, ease of laboratory testing compared to the burden of screening by interview, and the ability to provide better treatment options based on testing results [27]. It was recognized that screening is challenging in these circumstances due to drug use implications and child custody considerations, but the epidemiology involved in these diagnoses make early identification of infants at risk of the upmost importance [27].

As the incidence of NAS has increased dramatically in the last 14 years, there is no easy answer as to the best way to prevent harm to the infant while protecting the mother from legal implications and stigmatization. A positive drug screen has effects not only on the mother and her infant, but on the entire family including spouses, parents, and extended family [8]. If a child is removed from custody due to substance use disorder, this can create more trauma as social services works to find temporary custody with other family members, friends, or foster care. This can even create more harm to the mother and her child and can result in increased stress and psychological damage [8]. Substance use disorder should be seen as a medical issue that can be treated clinically rather than a criminal act. By providing women with un-biased treatment options and focusing on health outcomes, fear of punishment and feelings of guilt or shame can be reduced [8]. Pregnancy provides a unique opportunity for women to engage in treatment options as all pregnant women in the United States are eligible for Medicaid and women are often more motivated to accept treatment due to concern for their infant's health [29].

Withdrawal assessment tools and risk based screening are not new practices, but the rise in opiate-abuse during pregnancy and harm from withdrawal requires a more effective way to screen all infants. Selective drug screening is only cost-effective when the risk factors are efficient and specific [7]. As this research has shown, risk based screening was not efficient. Although universal screening would require an increase in upfront cost, the overall improvement in health outcomes would be cost-saving in the long term [28]. By standardizing risk based screening and/or implementing universal screening of all mothers during pregnancy or infants after birth, withdrawal and treatment can be improved and patients can be provided the best outcomes.

There are many social and ethical concerns involved in maternal and infant drug testing that cannot be ignored when considering prenatal and infant drug screening. Women recognized that the largest barrier to seeking treatment while pregnant was the fear of stigmatization [29]. They perceived judgment from healthcare providers, family, friends, and the addiction community itself, which often lead to poor self-esteem, shame, guilt, depression, relapse, and even death [29]. Ideally, substance use disorder would be treated as a medical issue where women could receive medical care, treatment, and resources without fear of punishment or stigmatization. In order to improve outcomes in women and children, there should be no downside to diagnosing substance use disorder in pregnancy, and the mother as well as the entire family should be considered in order to prevent harm and provide best outcomes for all.

DATA AVAILABILITY

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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AUTHOR CONTRIBUTIONS

AJK was the principal investigator in this study and was responsible for the concept and design of the study, the IRB application, collection of data and statistical analysis, figure and table creation, and was the sole writer of the manuscript and made all revisions in collaboration with the co-authors. MKR provided substantial contributions to the acquisition of data, statistical analysis, and interpretation of data. She also was involved in the revisions to improve intellectual content. LKS provided substantial contributions to the concept and design of this study and the acquisition of data. She also was involved in the revisions to improve intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

An IRB application was submitted to the University of Kentucky's and Baptist Health Lexington's IRB and both were approved in September 2019, including a waiver of informed consent.

CONFLICT OF INTEREST

The authors declare no competing interests.

ADDITIONAL INFORMATION

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