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Post-discharge healthcare utilization in infants with neonatal opioid withdrawal syndrome

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Abstract

The opioid epidemic in the United States has led to a significant increase in the incidence of neonatal opioid withdrawal syndrome (NOWS); however, the understanding of long-term consequences of NOWS is limited. The objective of this study was to evaluate post-discharge healthcare utilization in infants with NOWS and examine the association between NOWS severity and healthcare utilization. A retrospective cohort design was used to ascertain healthcare utilization in the first year after birth-related discharge using the CERNER Health Facts® database. ICD-9/ICD-10 diagnostic codes were used to identify live births and to classify infants into two study groups: NOWS and uncomplicated births (a 25% random sample). Evaluated outcomes included rehospitalization, emergency department (ED) visits within 30-days and one-year after discharge, and a composite one-year utilization event (either hospitalization or emergency department visit during that year). NOWS severity was operationalized as pharmacologic treatment, length of hospitalization, and medical conditions often associated with NOWS. In 3,526 infants with NOWS (restricted to gestational age \geq 33 weeks), NOWS severity was associated with an increase in composite one-year utilization (OR: 1.1; 95% CI: 1.04–1.2) after adjusting for prematurity, sepsis, jaundice, use of antibiotics, infant sex, insurance status, race, hospital bed size, year of birth, and census division. In a subset of full-term infants (3,008

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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with NOWS and 88,452 uncomplicated births), having a NOWS diagnosis was associated with higher odds of a 30-day (OR: 1.6; 95% CI: 1.03–2.4) and one-year rehospitalization (OR: 1.6; 95% CI: 1.1–2.4) after adjusting for infant sex, race, type of medical insurance, hospital location, census division, year of primary encounter, hospital bed size, and medical conditions. This study found higher healthcare utilization during the first year of life in infants diagnosed with NOWS, especially those with severe NOWS. Findings suggest a need for closer post-discharge follow-up and management of infants with NOWS.

Keywords

Neonatal opioid withdrawal syndrome; opioids; pregnancy; infants; hospitalizations; healthcare utilization

Introduction

Prevalence of opioid use disorder (OUD) at delivery hospitalization has increased from 1.6 to 6.5 per 1000 between 1999–2014.¹ Infants born to women with OUD are at risk for the Neonatal Opioid Withdrawal Syndrome (NOWS), also known as Neonatal Abstinence Syndrome (NAS), characterized by neurological, gastrointestinal, metabolic, and respiratory symptoms.^{2–4} While NAS symptoms might greatly vary among patients, it is a generalized term used to describe physiologic and/or behavioral dysregulation in the four key domains (i.e., state control/attention, motor and tone control, sensory processing, and autonomic control),⁵ which are not specifically attributable to a particular prenatal substance exposure. NOWS, while often used interchangeably with NAS, is the term intended to describe symptoms of withdrawal attributed specifically to prenatal opioid exposure.^{2,6} In reality, polysubstance use is very prevalent contributing to neurobehavioral dysregulation observed in the infant.⁷ While the term NOWS is widely used, there is no gold standard clinical or surveillance definition for NOWS and treatment. Various clinical scoring tools are used to indicate NOWS severity and guide treatment.^{7,8} Infants with NOWS may have prolonged hospitalization and require non-pharmacologic management as well as often times requiring pharmacologic interventions.^{2–4,9} NOWS also has a significant economic burden; cost of treating a NOWS infant was estimated at \$16,893 compared to \$5,610 for non-NOWS infant and the total cost of NOWS birth covered by Medicaid was \$462 million in 2014 with \$1.5 billion in hospital charges each year in the United States.^{10–12}

The knowledge on long-term effects of NOWS on infant and child health outcome is limited. There are inconsistent findings on the impact of prenatal opioid exposure associated NOWS on birth defects^{13–15}, anthropometric measures,^{16–18} and neurodevelopment^{19–22}. While clinical guidelines for the management of NOWS during the initial delivery hospitalization have received a lot of interest lately, information on the medical needs of infants with NOWS^{2,6} and healthcare utilization during the first year of life is limited. In addition to the effects of prenatal opioid exposure, infants born into households with low socioeconomic status may also be exposed to poor nutrition related to delayed or poor breastfeeding, unstable guardianship, and lack of or limited follow up care.^{26–29} Recent studies have indicated higher healthcare utilization rates in early years of their life,^{23,24,30} however,

analyses were limited to specific geographic regions or a specific type of healthcare utilization (e.g., only rehospitalization^{23,30}). To our knowledge, no prior studies have examined the possible association between the severity of NOWS (including complications in the neonatal period secondary to NOWS and the need for pharmacologic interventions) and post-discharge healthcare utilization. The increase in incidence of NOWS in recent years warrants a detailed study of its long-term impact on infants. Evidence from such long-term studies can be translated to inform policies that reduce adverse health outcome and provide additional support and services to the mother-infant dyad. To that end, the overall objective of the study was to examine the incremental use of acute healthcare in infants with NOWS compared to infants with uncomplicated births during a one-year follow-up after the hospital discharge using a large nationally representative clinical database. Furthermore, this study examined the association between NOWS severity and post-discharge healthcare utilization.

Methods

Study design and population:

The study population consisted of singleton live births discharged between January 1, 2011, and October 31, 2016. The retrospective cohort design utilized the Health Facts[®](HF) database containing extensive clinical data across 800 U.S. hospitals and healthcare systems that use the CERNER Electronic Health Record (EHR) system. HF includes encounter data for emergency department (ED), and inpatient visits. Continuity of patient encounters occurring within the same health system is preserved. Healthcare utilization during the 30-day and one-year (365 days) period after hospital discharge following birth hospitalization was evaluated. The International Classification of Diseases Ninth Revision Clinical Modification (ICD-9-CM) and Tenth Revision (ICD-10-CM) diagnosis codes were utilized to classify subjects into groups. The University of New Mexico Human Research Review Committee approved the study.

Primary eligibility criteria (for both study groups): Live births were identified using the ICD-9/10-CM diagnosis codes (Appendix Table A.1). Infants whose age at the beginning of the initial hospital stay (birth or the first recorded event in the HF database) was more than four days (to avoid any cases of readmissions), infants who expired, were transferred to a different facility, or had length of stay more than 60 days were excluded. Length of stay more than 60 days was an exclusionary criterion since such prolonged hospitalization could be due to complications unrelated to NOWS. Additionally, infant age at discharge would be substantially different between the study groups making the comparison difficult.

Eligibility criteria for infants with NOWS: Infants with 1) gestational age \geq 33 weeks; 2) initial length-of-stay (LOS) \geq 3 and $<$ 60 days; and 3) diagnosis codes 779.5 (ICD-9-CM) or P96.1 (ICD-10-CM,) corresponding to drug withdrawal syndrome in infants.^{31,32} The positive predictive value of these ICD-9-CM and ICD-10-CM codes for identifying infants with NOWS is 91% and 98.2%, respectively.³² We excluded infants whose initial LOS after birth was less than three days to ensure that all infants had at least 72 hours of observation for withdrawal symptoms to manifest – an eligibility criterion consistent with prior studies.^{4,32} Infants with suspected iatrogenic NOWS not due to *in utero* opioid exposure were

excluded (diagnosis codes listed in Appendix Table A.1).^{9,23} For the comparison with uncomplicated term-born infants, Nows infants who had late-preterm birth (gestation age 33 weeks to <37 weeks) were excluded using ICD-9/10-CM diagnosis codes (Appendix Table A.1).

Eligibility criteria for control group (uncomplicated term-birth

infants): Uncomplicated term-birth infants were identified as infants who met the primary eligibility criteria. Infants with Nows or iatrogenic Nows codes, LOS >3 days, or preterm infants (gestational age <37 weeks) were excluded. Of the infants who met primary eligibility criteria summarized above, a random 25% sample was selected to be included in analyses.

Materials and Measures:

Measures of post-discharge healthcare utilization in infants and

covariates: Evaluated outcomes included hospital readmissions, and emergency department (ED) visits occurring 30 days and one year from the birth hospitalization discharge date. For the analysis measuring the association of severity with post-discharge health care utilization, we used a combined measure – any ED visit or hospital readmission in the study period.

Covariates included sociodemographic characteristics (infant sex, race, type of medical insurance), birthing hospital characteristics (hospital location [urban vs. rural], census division, hospital bed size), year of primary encounter, and noted medical conditions during the birth hospitalization (e.g., respiratory problems, feeding difficulties, jaundice, sepsis) [Appendix Table A.1]). These medical conditions were previously found to increase the risk of rehospitalizations in the pediatric population.³³

Nows severity measures: Nows severity measures included the need for pharmacologic treatment (i.e., morphine, methadone, tincture of opium, phenobarbital), LOS, other medication use (i.e., benzodiazepine),³⁴ and presence of medical conditions often associated with Nows (i.e., respiratory problems, convulsions/seizures, feeding difficulties) – common measures utilized in prior studies.^{2,35}

Statistical analyses:

T-tests and chi-square tests assessed baseline differences between the Nows and uncomplicated birth groups for continuous and categorical variables, respectively. Logistic regression was used to assess the post-discharge healthcare utilization in infants with Nows compared to controls (term-birth Nows infants compared to uncomplicated birth group as a reference) before and after adjusting for covariates listed earlier.

The association between individual Nows severity measures and a composite one-year utilization event (defined as either hospitalization or emergency department visit during that year) was examined using logistic regression. As many of the factors were strongly correlated, principal component analysis – a dimensionality reduction technique, was used to create uncorrelated components as composite measures of Nows severity. Principal

components were derived using the following: pharmacological management of NOWS, LOS, respiratory conditions, feeding difficulties, and use of benzodiazepines. Components were retained based on Kaiser criteria of eigenvalue > 1 .³⁶ Component factor scores were estimated for each infant. These were used in the logistic regression to examine the association between principal components and the composite healthcare utilization event. Multivariable model included adjustment for prematurity, sepsis, jaundice, use of antibiotics, infant sex, insurance status, race, hospital bed size, year of birth, and census division.

Each of the analyses contained: 1) an unadjusted model, and 2) a model adjusted for measured covariates. Odds ratios (OR) and 95% confidence intervals (CI) were estimated. Clustered robust standard errors were used to account for the potential lack of independence between births occurring within the same hospital.³⁷

Results

We identified 3,526 infants with NOWS between January 1, 2011 and October 31, 2016. From 355,875 infants who met uncomplicated birth criteria during the same period, a 25% random sample was selected, and after exclusion of duplicates, 88,452 subjects were retained.

The NOWS incidence rate was 5.9 per 1000 births in 2011 and 13.1 per 1000 births in 2016, a 120% increase in 5 years. At baseline, significant differences were observed across groups regarding sex, race, insurance type, birth census region, urban/rural hospital status, and hospital size (all p-values < 0.05 ; Table 1). In the NOWS group, approximately 34% received inpatient pharmacologic treatment. Of the 3,526 NOWS infants, 3,008 were full-term (> 37 gestational weeks).

Post-discharge health care utilization in infants with NOWS vs. controls (full-term infants in both groups):

One-year rehospitalization was significantly higher in the NOWS group (3.8%) compared to the controls (1.6%, $p < 0.001$; Table 2). Similarly, the incidence of an ED visit during the first year after birth hospitalization discharge was higher in the NOWS groups (7.3%) compared to controls (6.1%, $p < 0.001$). The NOWS group also had higher rates of 30-day rehospitalization (2.4%) and ED visits (1.9%) compared to the uncomplicated birth group (rehospitalization: 0.9%; ED visit: 1.6%; $p < 0.001$ for both).

The likelihood of rehospitalization was higher for the NOWS compared to the uncomplicated birth group, with similar ORs estimated for both one-year and 30-day events (Table 3). For infants with NOWS, the unadjusted OR was 2.5 for one-year rehospitalization (95% CI: 1.9–3.3), and 2.7 for 30-day rehospitalization (95% CI: 1.9–3.8). After adjustment for measured covariates, the OR was 1.6 for both one-year (95% CI: 1.1–2.4) and 30-day rehospitalization (95% CI: 1.0–2.4). Unadjusted and adjusted OR estimates for any post-discharge ED visit were not significant. However, the OR estimate for the combined event of any ED visit or rehospitalization was significant in unadjusted models (one-year, 95% CI: 1.1–1.9; 30-day, 95% CI: 1.3–2.3), but not after adjustment for covariates.

NOWS-related severity measures and post-discharge composite event (infants with NOWS 33 weeks gestation):

Among infants with NOWS, those receiving pharmacologic treatment had longer LOS compare to those that did not require pharmacologic treatment (mean: 21.8 days vs. 11.4 days, $p<0.001$; median: 19 days vs. 7 days), a higher incidence of respiratory issues (27.5% vs. 17.4%, $p<0.001$), and more feeding difficulties (26.2% vs. 14.4%, $p<0.001$) (Appendix Table A.2). In unadjusted analyses of individual NOWS severity measures, greater odds of a composite one-year healthcare utilization event were associated with administration of benzodiazepines, and presence of any respiratory condition (also significant for 30-day event) (Figure 1).

Results of principal component analyses identified three principal components as weighted measures of NOWS severity. Component 1 was positively and heavily loaded with pharmacologic treatment, LOS, and feeding problems (Appendix Table A.3), indicating infants with a high factor score for Component 1 will have been treated for NOWS, have longer LOS, and have feeding problems. Component 2 served to summarize infants with feeding problems, not treated for NOWS, and with no benzodiazepine use. Finally, Component 3 was a summary measure for infants with transient tachypnea, but without respiratory distress syndrome, unspecified respiratory condition, or other specified respiratory conditions.

There were significant associations between factor score for Component 1 and a 30-day composite visit (OR: 1.2; 95% CI: 1.1–1.3), and a one-year composite visit (OR: 1.2; 95% CI: 1.1–1.2) in unadjusted analyses (Table 4). After adjusting for infant sex, race, type of medical insurance, hospital location, census division, year of primary encounter, hospital bed size, and noted medical conditions, only the association for Component 1 with the one-year composite visit remained significant (OR: 1.1; 95% CI: 1.04–1.2), however the 30-day estimate for Component 1 and estimates for Component 2 were marginally significant. No significant relationship was found between Component 3 and composite events.

Discussion

Infants with NOWS differed significantly in their baseline characteristics compared to infants in the uncomplicated birth group. A higher proportion were Caucasian (80.5% vs. 57.0%) and covered by Medicaid (68.4% vs. 34.3%), which is consistent with previous reports.^{38–41} This study demonstrated an increased risk of rehospitalization during the first year of life for infants with NOWS, which is consistent with other studies. A previous report, which retrospectively reviewed readmissions for 1,900 infants with NAS in Washington State (years 1990–2008), did not report one-year rates, but observed a higher risk of a five-year hospital readmission (adjusted relative risk: 1.54; 95% CI 1.37–1.73).²⁴ Similarly, a New York state inpatient database study (years 2006–2009) observed 30-day rehospitalization rates of 3.0% in NOWS vs. 1.9% in the uncomplicated birth groups, with a wider gap by one-year follow-up (NOWS: 7.7%, uncomplicated birth: 4.0%).²³ Absolute readmission rates for the NOWS group in our study were lower compared to the New York estimates reported by Patrick *et al.*,²³ but relative differences for a 30-day readmission between the NOWS and uncomplicated birth groups were similar (adjusted OR=1.6 in our

study vs. 2.5 in Patrick *et al.*). A recent study by Liu *et al.* using a U.S. commercial claims database (years 2005–2015) also reported higher numbers of claims for inpatient stays and ED visits 4–12 months post-discharge in infants with NOWS compared to children without NOWS.²⁵ A population-based retrospective study from New South Wales found that infants with NOWS had a higher risk of hospitalizations (OR=1.6) using a population-based retrospective cohort study.³⁰ While not specific to infants with NOWS, Raitasalo *et al.* reported higher rates of injury, infectious diseases, hospital treatment for other reasons in children born to women with substance use disorders in a study performed in Finland.⁴² These studies support the finding that infants with NOWS are at high-risk of needing rehospitalization and health care utilization.

Thirty-four percent of the infants in this study received pharmacologic treatment for NOWS. Our observed rates of NOWS treatment were lower than those reported by most prior studies.^{43–47} Infants receiving pharmacologic treatment in our study had longer LOS and higher rates of respiratory problems, convulsions/seizures, feeding difficulties, and sepsis. It is important to consider that some of these diagnoses could be due to the pharmacologic management of NOWS and related adverse effects of medication (e.g., over-sedation with resultant feeding difficulties or respiratory problems). In infants with NOWS, the presence of respiratory problems during the initial hospital stay was consistently linked with higher post-discharge healthcare utilization, which may reflect the need for management after discharge of the respiratory problem. We have previously reported a median LOS of 4.5 days in infants born to women with OUD at our facility who did not receive pharmacologic treatment for NOWS,²² a LOS that is similar to the average LOS of 5 days reported by Corr and Hollenbeak for non NAS infants.¹⁰ In this study infants who did not receive pharmacologic treatment had a median LOS of 7 days, compared to 19 for infants receiving treatments. The median LOS in this study may be higher due to the study minimum stay requirement. Of note, Corr and Hollenbeak reported a similar LOS difference between treated and not treated groups (10.6–12.3 days).¹⁰

A primary strength of this study is the large nationally representative sample from more than 800 hospitals across the country with the inclusion of all payers – commercial, Medicaid, and self-pay. This represents a substantial improvement over previous study designs which relied on state-specific or commercial claims data and improves the generalizability of the results.^{23–25} Second, this study benefits from an examination of both 30-day and one-year outcome measures as well as the robustness of the outcomes evaluated as ED visits, and rehospitalizations. Third, the study included a robust sample of infants with NOWS (n=3,526) ascertained over five years. Finally, this is the first study linking NOWS severity to post-discharge healthcare utilization.

While results observed in this study are consistent with previous findings, absolute healthcare utilization measures tended to be lower, potentially due to study inclusion criteria. ICD-9/ICD-10 diagnostic codes were used to identify infants with NOWS. However, ICD codes used in administrative data are subject to institutional variability. To adjust for this potential bias, we used robust cluster analysis to account for such variability among the hospitals. Our exclusion of infants with LOS <3 days or >60 days may have contributed to lower readmission rates. In the New York State Inpatient Database study, infants with

NOWS with an initial LOS <7 days were found to have higher rates of rehospitalization compared to those with longer hospital stays.²³ Consistent with established practice, we used a minimum of 3 days for the initial LOS. Additionally, we purposively excluded pre-term infants from comparisons with infants with uncomplicated births since prematurity is a known strong confounder. In these analyses our objective was to examine any incremental differences between term-birth infants with NOWS and infants with uncomplicated births.

There were other limitations to our study. Similar to other pediatric readmission studies, our study is limited by incomplete readmission information since we used hospitalization data for the Cerner EHR facilities.^{49–51} It has been estimated that 14–15% of pediatric readmissions in a 5-year period do not occur at the same hospital.⁵⁰ Our data did not allow linkage with maternal health information, which is an important confounder in healthcare utilization. Our study also lacked outpatient treatment information which could have led to lower estimates of infants with NOWS requiring pharmacological treatment. The effect of specific pharmacologic treatment could not be evaluated as the dosing information could not be reliably abstracted. We evaluated multiple types of post-discharge outcomes; however, recurrent visits are not independent events; infants with an ED visit might be more likely to have another event. Marginal structural models could be used to address the dependency between post-discharge events in the future.⁵⁴ It is also important to note that while our findings suggest a strong association between NOWS and increased post-discharge health care utilization, it does not imply causation. Future research could benefit from addressing the limitations of the study.

Conclusion

Newborns with NOWS are at risk for increased short- and long-term adverse outcomes. Other aspects to consider related to adverse outcomes include difficulty caring for the newborn due to effects of NOWS (which can continue for many weeks after discharge),⁵⁵ maternal factors,^{56,57} and an adverse social environment.⁵⁸ Based on the findings presented here, interventions such as home visiting, case management, lactation support, and efforts targeting attendance of scheduled newborn follow-up or well-child visits, may be warranted for infants with a history of NOWS or *in utero* opioid exposure in order to minimize preventable and unplanned healthcare utilization. Interventions should also focus on maternal health and substance use treatment along with assistance for women in the postpartum period to reduce relapse and promote healthy home environment for the mother-infant dyad. While some institutions are developing their own guidelines for post-discharge follow up of infants with NOWS, it is important to develop national recommendations so that all infants with NOWS have appropriate follow up to optimize their outcomes. The development on newer approaches towards the management of NOWS, such as the East-Sleep-Console, also could affect post-discharge healthcare utilization, and warrants additional research.⁵³

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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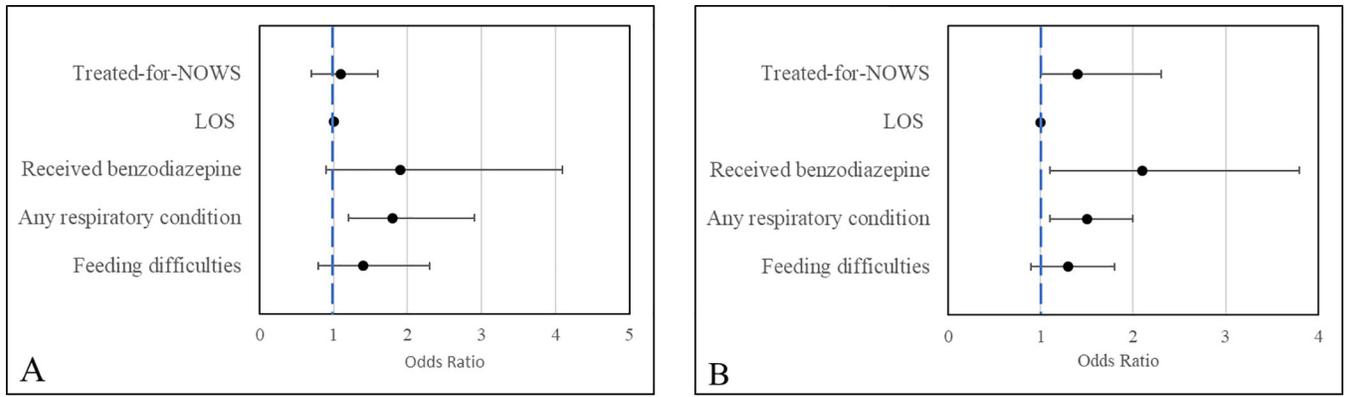
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Highlights

- Limited research on long-term effects of NOWS
- CERNER Health Facts® database from 800 healthcare systems used
- Infants with NOWS are at risk of 30-day and one-year rehospitalizations vs. controls
- NOWS severity associated with increased healthcare utilization during first year
- Planned post-discharge follow up recommended to minimize unintended hospitalization



A: 30-day utilization, B: One-year utilization

Figure 1. Association between Individual NOWS Severity Measures and Composite Healthcare Utilization (ED visit or rehospitalization).

Table 1:

Description of demographic, medical and patient care setting characteristics by study group

Variable	NOWS (term-birth) (n=3,008)	Uncomplicated term-birth (n=88,452)	p-value
Sex			0.042
Male	52.5%	50.6%	
Female	47.5%	49.4%	
Race			<0.001
Caucasian	80.5%	57.0%	
African American	5.2%	14.1%	
Hispanic	0.7%	2.8%	
Native American	2.8%	1.2%	
Other	10.8%	24.9%	
Insurance Type			<0.001
Medicaid/Medicaid MC	68.4%	34.3%	
Commercial	11.9%	44.4%	
Other	19.7%	21.4%	
Census region			<0.001
Midwest	15.9%	22.9%	
Northeast	46.2%	33.1%	
South	23.2%	28.1%	
West	14.6%	16.0%	
Rural/Urban Status			0.007
Rural	15.1%	17.0%	
Urban	84.9%	83.0%	
Bed size range			<0.001
Less than 100	7.4%	13.3%	
100–299	28.6%	37.6%	
Greater than 300	64.1%	49.1%	
Year			<0.001
2011	9.4%	15.0%	
2012	12.0%	15.2%	
2013	15.1%	18.0%	
2014	23.3%	19.5%	
2015	20.5%	18.4%	
2016	19.9%	14.0%	
<i>Noted medical conditions</i>			
Any respiratory problems	18.1%	2.6%	<0.001
Type of respiratory problems:			
Respiratory distress syndrome	3.5%	0.2%	
Transient tachypnea of newborn	10.4%	1.5%	
Respiratory condition of newborn (unspecified)	0.8%	0.1%	

Variable	NOWS (term-birth) (n=3,008)	Uncomplicated term-birth (n=88,452)	p-value
Other specified respiratory condition	6.3%	1.1%	
Convulsions	1.2%	0.1%	<0.001
Feeding difficulties	16.3%	1.0%	<0.001
Jaundice	32.1%	10.9%	<0.001
Sepsis	4.3%	0.4%	<0.001
LOS, mean (SD), days	14.6±11.7	2.1±0.8	<0.001
NOWS treatment			
(Both term and late-preterm NOWS infants)	(n=3,526)		
Treated-for-NOWS	34.0%	-	
Received morphine	24.7%	-	
Received methadone	7.9%	-	
Received morphine or methadone	31.2%	-	
Received phenobarbital	6.4%	-	

LOS, length-of-stay; SD, standard deviation, MC, Managed Care

Table 2:

Post-discharge healthcare utilization by study group

Variable	NOWS (term-birth) (n=3,008)	Uncomplicated term-birth (n=88,452)	p-value
<i>Rehospitalization</i>			
Events in one-year, any	3.8%	1.6%	<0.001
Events in 30-days, any	2.4%	0.9%	<0.001
<i>Emergency Department visit</i>			
Events in one-year, any	7.3%	6.1%	<0.001
Events in 30-days, any	1.9%	1.6%	<0.001
<i>Rehospitalization or Emergency Department Visit</i>			
Events in one-year, any	10.2%	7.3%	<0.001
Events in 30-days, any	4.2%	2.4%	<0.001

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Table 3:

Risk of post-discharge healthcare utilization in the term-birth NOWS group compared to controls during the one-year follow-up period: results from logistic regression modeling.^a

Healthcare utilization outcomes	OR	95%CI	p-value
<i>One-year emergency department visit</i>			
Unadjusted model	1.2	0.9–1.7	0.248
Adjusted model *	0.8	0.6–1.1	0.220
<i>30-day emergency department visit</i>			
Unadjusted model	1.2	0.9–1.7	0.258
Adjusted model *	0.9	0.7–1.2	0.342
<i>One-year rehospitalization</i>			
Unadjusted model	2.5	1.9–3.3	<0.01
Adjusted model *	1.6	1.1–2.4	0.013
<i>30-day rehospitalization</i>			
Unadjusted model	2.7	1.9–3.9	<0.01
Adjusted model *	1.6	1.0–2.4	0.036
<i>One year any visit (ED or rehospitalization)</i>			
Unadjusted model	1.4	1.1–1.9	0.004
Adjusted model *	1.0	0.8–1.2	0.806
<i>30-day any visit (ED or rehospitalization)</i>			
Unadjusted model	1.7	1.3–2.3	<0.01
Adjusted model *	1.2	0.9–1.5	0.318

^aAnalyses restricted to full-term infants in both study groups.

* Adjusted for infant sex, race, type of medical insurance, hospital location, census division, year of primary encounter, hospital bed size, and noted medical conditions.

Table 4:

Association between post-discharge healthcare utilization (composite outcome) and principal components of NOWS severity measures (N=3,526): Results of multivariable logistic regression^a

	Composite healthcare utilization measure ^b			
	One-year visit		30-day visit	
	OR (95% CI)			
	Unadjusted	Adjusted ^c	Unadjusted	Adjusted ^c
Component NOWS severity measures^d				
Component1	1.2 (1.1–1.2)*	1.1 (1.04–1.2)*	1.2 (1.1–1.3)*	1.1 (0.99–1.3)
Component2	1.0 (0.9–1.1)	1.1 (0.9–1.1)	1.0 (0.98–1.3)	1.1 (0.95–1.2)
Component3	1.0 (0.9–1.1)	0.9 (0.9–1.03)	1.0 (0.9–1.1)	1.0 (0.8–1.2)

^aLimited to the NOWS group with gestational age \geq 33 gestational weeks.

^bComposite healthcare utilization included either emergency department visit or hospitalization

^cAdjusted for prematurity, sepsis, jaundice, use of antibiotics, infant sex, insurance status, race, hospital bed size, year of birth, and census division

^dPrincipal component measures selected based on Kaiser criteria, eigenvalue $>$ 1, factor loadings for the principal components are shown in Appendix Table A.3

* p<0.05