


Pediatric Pharmacy Advocacy Group

Shake, Rattle, and Roll: NAS Management in Ambulatory Care

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Disclosures


- No conflicts of interest to disclose



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Objectives

1. Discuss challenges of monitoring neonatal abstinence syndrome (NAS) in the ambulatory care environment
2. Review the advantages and disadvantages of treatment options for the management of NAS in the outpatient setting
3. Identify trials faced by parents when caring for a child with NAS at home
4. Using a patient case, follow the course of NAS managed solely in the outpatient setting



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Neonatal Abstinence Syndrome (NAS)

- Incidence ↑ from 1.2 to 3.39 infants/1000 hospital births annually between 2000 to 2009
- Onset time for NAS:

Drug	Onset, hours	Frequency, %
Heroin	24-48	40-80
Methadone	48-72	13-94
Buprenorphine	36-60	22-67
Prescription opioid meds	36-72	5-20
Selective serotonin reuptake inhibitors	24-48	20-30
Tricyclic antidepressants	24-48	20-50
Methamphetamines	24	2-49

- 60-80% will require pharmacologic treatment

Patrick SW, et al. JAMA 2012;307:1934-40.
Tolia VN, et al. NEJM 2013;372:2138-26.
Kocherlakota P. Pediatrics 2014;134:e647-61.



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Management of NAS

- Management typically occurs in inpatient setting
 - AAP recommends to observe for 3-7 days
 - Accounts for 4% of US NICU admissions
 - Average inpatient length of stay of 17-23 days
- Pharmacologic therapy if inadequate response to non-pharmacologic therapy
 - Morphine & methadone most commonly used
 - Approximately 1/3 of NICUs DC patients home on NAS treatment

Hudak ML, et al. Pediatrics 2012;129:e540-60.
Patrick SW, et al. J Perinatol 2015;35:650-5.
Mehta A, et al. Hosp Pediatr 2013;3:317-23.

AAP = American Academy of Pediatrics



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Disadvantages of Inpatient Management


- Burden on hospital resources
 - Occupy NICU/General Ward bed space
 - Nursing time & attention
- Financial burden – cost >3-times non-NAS admission
- Separation of mother-baby dyad
- Stressful, regimented environment



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**WHAT IS KNOWN ABOUT THE
OUTPATIENT MANAGEMENT OF NAS**



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Outpatient Models of Care

- Managing Abstinence in Newborns (MAiN) program
- Outpatient, multidisciplinary clinic
- Off-site NAS withdrawal centers
- Home-based management




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MAiN Program – Outpatient Clinic

- Eligible patients:
 - Mother taking ≥ 20 mg methadone or ≥ 9 mg buprenorphine for ≥ 2 weeks
 - ≥ 35 weeks gestational age and no other conditions requiring NICU admission
- Program includes:
 - Methadone initiated within 24 hours of birth
 - Rooming-in with mother in low-acuity setting
 - Combined inpatient-outpatient wean


Dukes L, et al. Popul Health Manag 2017;20:458-64.
Hudson J, et al. Am J Pharmcase 2017;34:576-86.



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Outpatient Management

- Pharmacist develops calendar with taper plan
 - Dose ↓ by 15% of discharge dose every Sunday & Wednesday
 - Methadone dispensed in pre-filled syringes
- Caregivers required to fill prescription prior to discharge
- Outpatient clinic visits weekly
- Family asked to monitor symptoms, but do not formally score



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Results of MAiN Program (n=117)

- Medical outcomes:

Medical Outcomes	Median (range)	Mean (SD)
Length of stay (days)	8 (4-18)	8.3 ± 2.7
Methadone discharge dose (mg/kg/day)	0.4 (0.1-1.4)	0.5 ± 0.3
Duration of outpatient wean (days)	46 (10-96)	44.6 ± 16.3
Cumulative methadone outpatient dose (mg)	30 (3.1-160)	33.3 ± 25.4

- Safety outcomes:

Safety Outcomes	Number (%)
Outpatient adverse events	
Alteration of planned wean	23 (20)
Suspected mishandling of medication by caregiver	10 (9)
Lacked medication to complete wean	8 (7)
ED visit or readmission w/in 30 days of DC	16 (14)
Possibly NAS related	8 (7)
Not NAS related	8 (7)




Hudson J, et al. Am J Perinatol 2017;34:576-84.

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Financial Outcomes

Year	Managing Abstinence in Newborns Intervention	South Carolina	United States (data available for 2006, 2009-2012 only)
2006	~\$10,000	~\$30,000	~\$55,000
2007	~\$10,000	~\$50,000	-
2008	~\$10,000	~\$40,000	-
2009	~\$10,000	~\$35,000	~\$55,000
2010	~\$10,000	~\$55,000	~\$65,000
2011	~\$10,000	~\$45,000	-
2012	~\$10,000	~\$50,000	~\$70,000
2013	~\$10,000	~\$48,000	-
2014	~\$10,000	~\$52,000	-



Dickes L, et al. Popul Health Manag 2017;20:458-64.

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Factors of Successful Implementation

- Early methadone initiation (< 48 hrs of birth)

Maternal Medication/Dose	Neonate Methadone Dose
Methadone > 60 mg/day	0.1 mg/kg/dose every 6 hours
Methadone < 60 mg/day OR buprenorphine (any dose)	0.05 mg/kg/dose every 6 hours

- Reallocation of hospital resources for rooming in
- Dispensation of prefilled oral syringes
- Fill prescription prior to discharge
- Educate caregivers on signs of uncontrolled withdrawal that should prompt additional clinic visit
- LONG medication tapers



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Outpatient Clinic Safety & Sustainability

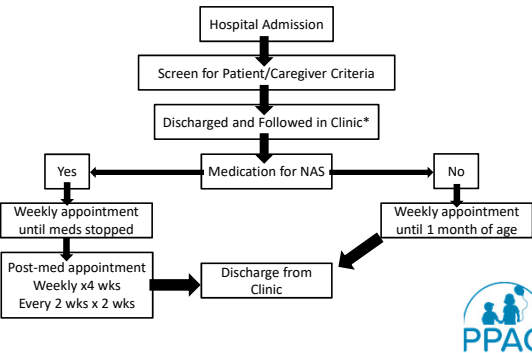
- Retrospective study of 774 infants followed in an outpatient clinic between 1998-2016
- Multi-disciplinary clinic staffed by 2 nurses, 2 neonatologists, & 1 pediatrician
- Mondays & Thursdays, 2-4 pm – first-come, first served basis
- Initial appointment within 3 days of discharge
- Dose adjustments based on caregiver reports



Rasul R, et al. Acta Paediatrica 2018;DOI: 10.1111/apa.14509

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Outpatient Clinic



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Results of Outpatient Clinic Model

- Clinic compliance > 95%
- 442 (58%) were exposed to opioids in-utero

Variable	Required NAS Treatment (n=239)	No NAS Treatment Required (n=203)
Inpatient LOS (days)	14 (9-23)	8
Discharged on NAS medication, n (%)	199 (83.3)	---
Median duration of morphine (days)	64 (35-110)	---
Duration of clinic follow-up (days)	77 (24-150)	21 (7-92)

- No NAS readmissions
- Three medication errors reported



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Factors of Successful Implementation

- No discharges on Friday or weekends
- Initial appointment shortly after discharge
- Prescribe medication quantities sufficient to last between clinic visits
- LONG medication tapers



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Off-Site Treatment Facility

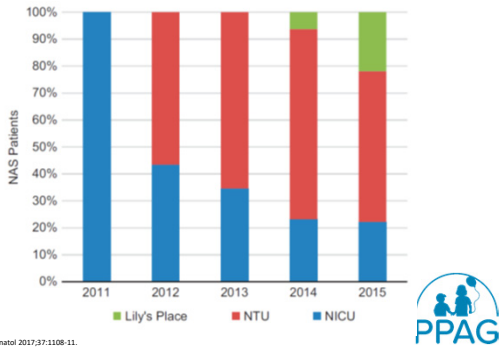
- July 2012 – established 15-bed Neonatal Therapeutic Unit (NTU)
- October 2014 – Off-site facility (Lily’s Place) opened as 12-bed neonatal abstinence center
 - Neonatologist, nurses, social worker, volunteers
 - Grant-funded and donation supported
- Protocol for management same in NTU, Lily’s Place, and NICU



Loudin S, et al. J Perinatol 2017;37:1108-11. <https://www.lilyplace.org/>

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Distribution of Admissions Over Time



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Comparison of Locations

- 78 patients treated at Lily's place between Oct 2014-Dec 2015

Location	LOS Median (IQR)	Avg Daily Charges per Patient	Median Charges per Patient
NICU	24 (24-52)	\$4,030	\$90,601
NTU	26 (26-42)	\$2,644	\$68,750
Lily's Place	33 (32-60)	\$400	\$17,688 ^a

^aLily's Place calculations include 1-3 day NTU stay



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Factors of Successful Implementation


- Facility for clinic
- Grant funding/donations
- Replication plans offered at www.lilysplace.org



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Caregiver Screening & Education

- Many studies refer to caregiver screening, but process not elucidated
 - Enrolled in treatment program (if applicable)
 - Stable living environment
 - Willingness to make frequent clinic visits
- Education provided:
 - Withdrawal symptoms
 - When to seek medical attention
 - Taper plan




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Self-Efficacy & Knowledge of Caregivers

- Descriptive, prospective study of caregivers w/ children receiving methadone (n=12)
- Pre-education confidence & knowledge:


Statement or Assessment	% Confident or % Correct
<i>Confidence Statements</i>	
Giving methadone as prescribed	83%
Identifying when to take child to PCP	75%
Identifying withdrawal symptoms	42%
<i>Knowledge Assessment</i>	
Correctly answered 100% of questions about symptom identification	8%
Correctly answered 75% of questions about symptom identification	25%



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Identified Concerns & Issues

Caregiver Concerns & Issues	n (%)
Confusion about purpose of taper	3 (25)
Concern about managing the taper at home	2 (16.7)
Misunderstanding of dosing terminology	1 (8.3)
Difficulty with pulling up and measuring oral liquid in observation session	5 (42)



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Summary of Outpatient Management

- Outpatient or combined inpatient/outpatient models of care have been described
- Patient selection/screening important
- Associated with shorter hospitalization times
- May be linked with greater lengths of therapy or higher rates of ED utilization
- Specialty clinic concept
- Role for the ambulatory care pharmacist

Murphy Oikonen J, et al. Primary Health Care Research & Development 2018. doi: 10.1017/S1469423618000270.
 Maslouf F, et al. J Pediatr 2018;199:151-7.
 Lee J, et al. Population Health Management 2015;18:392-7.
 Rasoul R, et al. Acta Paediatrica 2018. doi: 10.1111/apa.14509.
 Balakrishnan M, et al. Joint Commission Journal on Quality and Patient Safety 2018;44:309-11.



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CHALLENGES AND QUESTIONS: WHAT WE DO NOT KNOW ABOUT THE OUTPATIENT MANAGEMENT OF NAS



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Meet SG

PATIENT CASE EXAMPLE



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Prenatal History

- 26 year-old, G3P2 mother
- Mother contacted local, private adoption agency in 1st trimester with the intent for placement
- Some prenatal care obtained
- Mother hospitalized during pregnancy due to nausea and anxiety-related complaints
- Social concerns present prior to and during pregnancy
- Prenatal exposures
 - Alcohol in 1st trimester (unknown amount)
 - Marijuana daily throughout pregnancy
 - Buprenorphine and naloxone in 2nd/3rd trimester (unknown amount)



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Birth History

- Small, rural hospital
- Spontaneous vaginal delivery at 38⁴ weeks
- APGARs: 8 at 1 minute, 9 at 5 minutes
- Birthweight: 8lbs 3oz
- Urine drug screen: opiates positive
- Meconium drug screen:
 - Opiates positive
 - Cannabinoid positive



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Hospital History

- Uncomplicated hospital course
- Circumcision
- Modified Finnegan Neonatal Abstinence Scoring used by hospital staff
 - Scores \leq 4 for hospital course
 - No concerns of NAS noted by discharging provider
- Discharged at 48 hours with adoptive family
- Pediatrician follow-up on day of life 3



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NAS Presentation

- Signs and symptoms onset at days of life 4-5
- Modified Finnegan scoring elements present at ambulatory care visit on day of life 5

Excessive high-pitched cry < 5 mins	Sleeps < 1 hour after feeding
Hyperactive Moro reflex	Mild tremors
Increased muscle tone	Myoclonic jerks
Frequent yawning	Sneezing
Excessive sucking	Poor feeding (uncoordinated suck)
Regurgitation	Loose stools



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Next Steps

- What else would you like to know?
- What is next for SG?
- What would you do?



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CHALLENGES OF NAS MANAGEMENT IN AMBULATORY CARE



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Outpatient Presentation and Mgmt


- NAS presentation after hospital discharge
 - Management may involve hospital readmission
 - Pharmacy role in the transitions of care process and/or with caregiver support
- NAS inpatient/outpatient management model
 - More commonly seen and described
 - Significant role for ambulatory care pharmacist



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Exposures

- Most are not single substance exposures
- Exposures may have been unknown to hospital team
- Toxicological confirmation has a limited duration of detection based on substance
 - Urine (baby and/or mother)
 - Meconium
 - Umbilical cord or hair
- Detection depends on amount, duration, and method of administration plus the drug metabolism/clearance
- Delayed detection may prevent optimal treatment and create conflicts with and within the family




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Onset, Duration, & Frequency of NAS

Drug	Onset, hours	Frequency, %	Duration, days
Heroin	24-48	40-80	8-10
Methadone	48-72	13-94	≥ 30
Buprenorphine	36-60	22-67	≥ 28
Prescription opioid meds	36-72	5-20	10-30
SSRIs	24-48	20-30	2-6
TCA's	24-48	20-50	2-6
Methamphetamines	24	2-49	7-10
Inhalants	24-48	48	2-7

- NAS may present or symptoms worsen after hospital discharge



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NAS Monitoring

- NAS scoring systems (e.g., modified Finnegan)
- Used to assess NAS and to assist with monitoring, titrating, and terminating therapy
- Strong interobserver variability
- Scored after feeds, at 3- to 4-hour intervals when infant is awake
- Represents infant during entire time interval
- Not validated or recommend for caregiver use



Kocherlakota P, et al. Pediatrics. 2014;134(2):e547-e561.

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Monitoring in Ambulatory Care

- How do you monitor outpatient
 - Score the child for the time of visit?
 - Use caregiver reports?
 - Confounded by significant stimulation/change in environment at office compared to home
- How do you involve caregivers
 - What measures do you teach caregivers?
 - Confounded by health literacy, caregiver exhaustion, postpartum depression/anxiety



Janco M. Pediatric Academic Society Meeting 2018. Available at: <http://www.aappublications.org/news/2018/05/05/janco050518>. Accessed 2/2/19

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Non-Pharmacologic Management

- First option in all cases/should be taught to all
- Quiet, dark environment
- Avoid excessive handling or stimulation
- Swaddling
- Kangaroo care
- Frequent, on-demand feeding
- Breastfeeding (if not contraindicated)
- Pacifier use
- Continuous minimal stimulation practices (e.g., low noise, swing)
- Music or massage therapy




Kocherlakota P, et al. Pediatrics. 2014;134(2):e547-e561.

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Outpatient Pharmacologic Mgmt


- Typically part of an inpatient/outpatient treatment model
- Role of ambulatory care pharmacist
 - Confirm medication taper plan (may not exist)
 - Identify any health literacy challenges
 - Assure no medication procurement issues exist
 - Identify any health literacy barriers
 - Provide any support and education needed
 - Schedule close follow-up to keep on track



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Caregiver Trials in Medication Delivery

- Confidence/knowledge of taper or wean
- How to prepare correct dose
- What to do if a dose is missed
- Confidence/knowledge of withdrawal symptoms
- What to do if symptoms are present
- When to call/see the primary care provider
- Able to repeat information during teach-back
- Express understanding during teach-back




Capino AC, et al. J of Pharm Technol. 2016;32:104-15.

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Questions to Consider with ↑ Symptoms


- Medication adherence assessment
- Breast feeding status and any changes
- Changes in non-pharm management
- Other health-related issues in infant
- Changes in caregiver(s) or environment
- Changes in social situation of caregiver(s)
- Others



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Long-term NAS Monitoring


- Neurodevelopmental assessments
- Psycho-behavioral assessments
- Ophthalmologic assessments
- Growth and nutritional assessment
- Family support assessments



Kocherlakota P, et al. Pediatrics. 2014;134(2):e547-e561.

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PATIENT CASE FOLLOW-UP



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NAS Management – SG

- Managed outpatient with close follow-up
- Non-pharm management only
 - Dark, quiet room
 - On-demand feeding (various formulas)
 - Swaddling
 - Constant soothing noises
 - Baby swing
- Failed: donor breast milk and kangaroo care
- Averaged 2 in-office visits per week X 8 weeks



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Support Provided by Clinic Staff

- Education about NAS
- Options for management offered and discussed
- Monitoring parameters (specific for SG)
 - Excessive crying
 - Sleep after feeding
 - Tremors
 - Excessive sucking/feeding challenges
 - Loose, seedy stools/excoriation on bottom
- Support for family



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Working with Adoptive Families

- Who has legal custody and when (varies by state)
- Who is/are caregiver(s) inpatient and outpatient
- Will child be breast (birth or adoptive mother) and/or formula fed
- Health insurance
- Legal name at birth vs. given name by adoptive family vs. name on hospital paperwork
- Birthmother communication/open adoption



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Conclusions

- Incidence of NAS is on the rise
- Inpatient management is typical but has disadvantages
- Outpatient management models of care exist
- Challenges (e.g., caregiver screening, symptom monitoring, family support) must be addressed for successful outpatient care
- Pharmacy role in outpatient NAS care is vast



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