

Clinical Guideline:

Management of babies born to mothers who are on prescribed or misuse medications (opiate and related) leading to drug withdrawal features (Management of Neonatal Abstinence Syndrome (NAS)

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For use in:

EoE Neonatal Units Guidance specific to the care of neonatal patients.

Used by:

Neonatal Intensive Care Units East of England:

- Medical staff
- Nursing staff
- Paediatric Pharmacist

Key Words:

- Neonatal Abstinence Syndrome (NAS)
- Maternal drug misuse
- Infants of mothers on Methadone Programme
- Infants of mothers on prolong Opiates use for medical reasons
- Modified Finnegan Score (MFS)
- Medications: Opiates, Morphine; Clonidine; Phenobarbital

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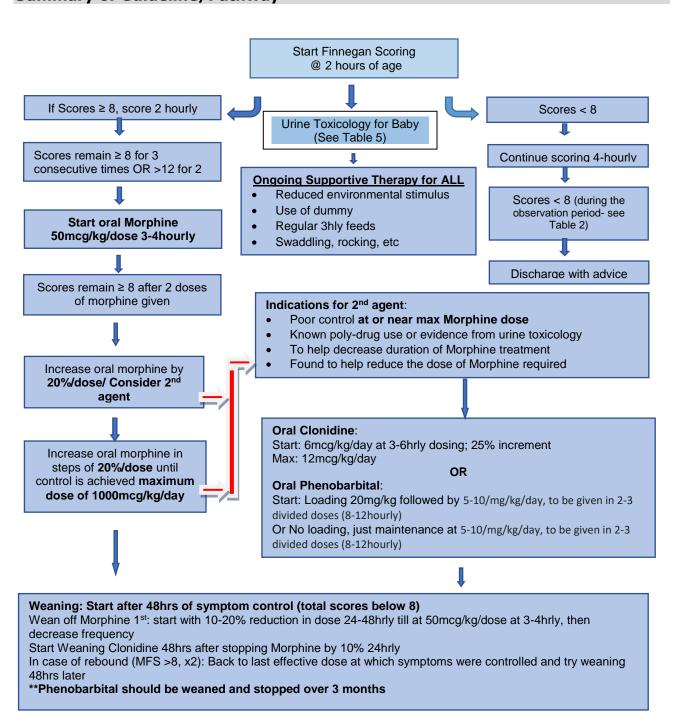


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Summary of Guideline/Pathway



Stop: Morphine 125mcg/kg/day or less; Clonidine at 1.5mcg/kg/day or less

Discharge: 48-72hrs after stopping medications

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Aims

- To standardise and outline good practice, using best evidence, in the postnatal management of babies whose mothers were known or suspected to have misused drugs during pregnancy or were on medications that may lead to withdrawal features in their babies
- To standardise the care plan between all professionals to meet the needs of the baby and family and ensure communication exists between all professionals, the family and their social support network
- Minimise the impact of withdrawal symptoms for the baby
- Provide appropriate neonatal care for the baby which facilitates maternal / infant bonding
- > The drugs included in this guidance are: opiates, cocaine, amphetamines, marijuana and poly-drug misuse (from afore mentioned list).
- ➤ **The guidance excludes**: management of babies whose mothers were on Mental Health-related medications, such as anti-psychotics and antidepressants (separate guidance under development).

Introduction

Intrauterine exposure during pregnancy, to certain illicit drugs or medications may lead to congenital anomalies and/or foetal growth restriction, increased risk of preterm birth, impaired neurodevelopment and increased rates of neonatal opioid withdrawal known as Neonatal Abstinence Syndrome (NAS), amongst others (Table 1). The exact number of drug-dependent women is unknown because the statistics rely heavily on voluntary patient disclosure. However, there is an increasing trend in the misuse of illicit drugs, as well as in prescribed medication, in pregnant women, nationally and internationally,

The most common and clinically important neonatal withdrawal commonly results from opioid exposure during pregnancy. Among neonates exposed to opioids in utero, withdrawal signs will develop in 55% to 94%. Neonatal withdrawal signs have also been described in infants exposed antenatally to other misused drugs/ maternal medications. (**Table 1**)

In certain cases, signs and symptoms of withdrawal worsen as drug levels decrease (for example, methadone, heroin), whereas signs and symptoms of acute toxicity subsides with drug elimination (cocaine). For most drugs, it is known that the risk and severity of NAS appears to be modified by opioid type and exposure to additional substances, such as maternal smoking and concomitant use of SSRI, sedatives-hypnotics, benzodiazepines, and by the time elapsed between last maternal use and delivery. However, this guidance does not include the management of babies exposed in-utero to anti-depressants and anti-psychotic medications.



<u>Table 1</u>: Maternal Misused Drugs and/or Medications and Known Outcomes

Drug/Medication	Known outcomes
Alcohol	Acute ingestion: Hyperactivity, tremors for 72 hours followed by lethargy for 48 hours Chronic ingestion: abnormalities include CNS, growth deficiency, facial features, cardiac and musculoskeletal anomalies (Foetal Alcohol Syndrome)
Amphetamines	Increased rate of abruption, IUGR, cardiac anomalies, intracranial lesions including infarcts and haemorrhage; agitation, hyperactivity
Benzodiazepines	'NAS-like' syndrome (neuro-behavioural dysregulation); hypothermia, hyperbilirubinaemia, CNS depression
Cocaine	Acute toxicity in newborn with agitation, tremors, difficulties with feeding, poor sleep; Neurological complications (brain infarcts, haemorrhagic lesions, cystic lesions); higher incidence of prematurity, low birth weight, placental abruption; associated with higher incidence of congenital genitourinary tract and gastrointestinal anomalies- ileal atresia; Short and/or long term neurobehavioral abnormality; limb reduction defects, NEC; myocardial infarction SIDS appear to be more common in cocaine exposed infants
Marijuana	Higher incidence of tremors and altered visual responses No withdrawal effects
Methamphetamines	IUGR, prematurity, placental abruption, foetal distress, adverse long- term neurotoxic effects on behaviour, cognitive skills, and physical dexterity
Opioids	NAS; Preterm labour; Low birth weight/ IUGR; Active/passive detoxification results in foetal distress or foetal loss; sleep deprivation;
(Incudes Methadone)	Increased risk of SIDS; No other adverse outcomes identified so far
Poly-drug use	Increased risk of abnormal pregnancy outcomes, greater risk of SIDS; Increased Infant mortality Rates; Associated with family and social issues

Neonatal Abstinence Syndrome (NAS)/ NAS- like Syndrome

NAS is an array of signs and neuro-behaviours experienced by the newborn that occur after abrupt discontinuation of pregnancy exposure to substances taken by the mother. The term NAS has been principally used to describe neonatal symptoms and signs occurring after prolonged in-utero exposure to opioids such as heroin, methadone, and buprenorphine, and use or misuse of prescription opioid containing medications, such as codeine. However, other substances may produce neuro-behavioural dysregulation in the neonatal period consistent with an abstinence/ withdrawal syndrome, including



benzodiazepines, alcohol, nicotine, and psychiatric medications such as antidepressants or antipsychotics.

Pathophysiology of NAS

The pathophysiology of NAS is rather complex and not well understood. However, altered levels of neurotransmitters are presumed to play a significant role due to abrupt cessation of trans-placental passage of opioid or other drugs/ medications exposure at birth.

Repeated exposure of opioid leads to increasing production of adenyl cyclase with further inhibition of C-AMP production. After removal of the opioid, the inhibition of adenyl cyclase is reversed, resulting in overproduction of C-AMP during subsequent withdrawal exposures. The resultant flux of C-AMP is suspected to cause the intense withdrawal manifestations, in addition to effects from dysregulation of other neurotransmitters.

Clinical features of NAS

This is variable and depends on: Type(s) of drug(s)/ Medication(s) taken, the amount taken, the pharmacokinetics of the drug, net transfer of drug across the placenta, placental metabolism, time between maternal drug use and infant delivery, maternal and infant metabolism and excretion, gestational age (GA) at birth and other unidentifiable factors.

Preterm infants have been described as being at lower risk of drug withdrawal with less severe and/or prolonged course of NAS with lower GA correlating with a lower risk of neonatal withdrawal and reduced adverse outcomes.

The apparent decreased severity of signs in preterm infants may relate to developmental immaturity of the CNS, differences in total drug exposure, or lower fat depots of drug. Furthermore, the clinical evaluation of the severity of abstinence may be more difficult in preterm infants, because scoring tools to describe withdrawal were largely developed in term or late preterm infants.

Table 3: Symptoms and Sign of Opioid Withdrawal

<u>rable 5</u> : Symptoms and Sign of Opiola Withdrawai		
CNS	Autonomic	GIT
Neurological excitability	Sweating	Poor feeding or excessive
with tremors, irritability,	Nasal stuffiness	feeding,
wakefulness, high-pitched	Sneezing	Uncoordinated and constant
cry,	Fever	sucking,
Hypertonia,	Mottling	Vomiting,
Hyperreflexia	Frequent yawning	Diarrhoea, dehydration
Exaggerated Moro's reflex.	Temperature instability Mild elevations in respiratory	Poor weight gain.
	rate and blood pressure	
	Seizures	

Table 4: 'Withdrawal' Features of other Drugs

<u>rable 4. Withdrawar reactives of other brugs</u>	
Cocaine &	Alcohol
Amphetamines (CNS	
stimulants)	
Irritability,	Hyperactivity, crying, irritability, poor suck, tremors,
Hyperactivity,	seizures;
Tremors,	onset of signs at birth, poor sleeping pattern, hyperphagia,



High pitched cry	Sweating
Excessive sucking	

When do symptoms/signs of NAS start?

Onset of withdrawal depends on the dose taken, half-life of the drug, duration of the addiction and time of last maternal dose prior to delivery. On average, observation period for symptoms to appear is about 24-72 hours (**Table 2**)

<u>Table 2</u>: Maternal Misused Drugs and/or Medications and Onset of Withdrawal symptoms

Drug	Appropriate time of onset
Alcohol	• 3-12hrs
Benzodiazepines	Few days to 3weeks
Cocaine	• 24-48hrs;
	Usually no withdrawal signs but
	neurobehavioral abnormalities (decreased
	arousal and physiologic stress)
Heroin (short half-life	Within 24 hours
Other Opioids	24-36 hours but can be up to 5-7 days
(buprenorphine (Subutex), codeine, Morphine,	
hydrocodone, hydromorphone, oxycodone, Pethidine)	
Methadone (long half-life)	 Within 3 days but up to 5-7 days;
	Rate of severity of withdraw does not
	correlate to maternal dose. Exposure is
	associated with longer duration of
	pharmacotherapy for NAS than Heroin
Methamphetamines	• 24-48hrs;
	Usually no withdrawal signs but
	neurobehavioral abnormalities (decreased
	arousal, increased physiologic stress, and
	poor quality of movement)
Marijuana	Usually no clinical withdrawal signs

Scoring System (See Appendix 1 for full details and key points)

Several scoring systems are available for use; however, the most widely validated and commonly used is the Finnegan Scoring System (Appendix 1). This 21-item scale, a modified version of the original created in 1975, evaluates multiple signs related to NAS and helps to guide treatment initiation and dosing. Scoring is to quantify the severity of symptoms to determine the need for pharmacologic intervention.

Literature shows that a standardised NAS scoring system is associated with a shorter length of stay and length of treatment. However, no studies to date have compared the use of different withdrawal score thresholds for initiating pharmacologic intervention on short-term outcomes.

Key points when scoring:

Due to its subjectivity the following Key Points should be borne in mind with the scoring:

➤ The first abstinence score should be recorded at approximately two hours after birth on infants with known in-utero drug exposure.



- > Scoring should be started upon suspicion of withdrawal (see table 3) in infants with unknown maternal drug history.
- Following the baseline score all infants should be scored at 4-hourly intervals if score remains <8</p>
- Scoring should reflect the baby's condition observed during the scoring interval, that is, since the last score was recorded, not just at the time of scoring and an assessment after a feed
- > In a term baby, scoring should be performed 30 minutes to one hour after a feed, before the baby falls asleep.
- > A crying infant should be soothed and quietened before assessing muscle tone, Moro reflex and respiratory rate.
- ➤ If the infant's score at any scoring interval is > 8, scoring is increased to 2-hourly and continued for 24 hours from the last total score of 8 or higher
- ➤ If the 2-hourly score is ≤7 for 24 hours then scoring intervals may change to 4-hourly
- ➤ If pharmacotherapy is required the infant is scored at 2 or 4-hourly intervals, depending on whether the abstinence score is less or greater than 8 throughout the duration of therapeutic period
- ➤ If, after cessation of pharmacotherapy the scores are persistently less than 8 for 24-48 hours then scoring may be discontinued and baby can be discharged home There should be formal training on the use of the MFS, organised by midwifery or neonatal training team, as stated by the authors of the MFS

Differential diagnosis

Certain conditions may mimic or confound NAS and therefore may require investigating to help rule out as a cause of the NAS-like presentation:

- > Infection.
- Hyperviscosity syndrome (from polycythaemia)
- > Metabolic disorders such as hypoglycaemia, hypocalcaemia, hypomagnesaemia
- > Jitteriness from metabolic disorders and polycythaemia
- > Hyperthyroidism
- Seizures ?cause
- > Intracranial pathology haemorrhage, ischaemia,
- Consideration should be given to NAS due to barbiturates and antidepressants such as SSRI

Investigations

The following babies may require the following investigation(s):

Table 5: List of suggested Investigations and Indications

Investigation	Indication
Urine toxicology - Send to biochemistry (use universal urine container) minimum 1 ml of urine from cotton wool pad placed in the	 All cases of maternal drug misuse/ methadone programme; Requested by Social services (SS) with documentation; Part of clinical care after consent from the mother
nappyTo be collected as soon as possible after birth, as many	**Results must take into account any prescribed drugs given to mother during labour



drugs are rapidly metabolized and eliminated	**Collection should follow a Chain of Custody (see Appendix 3 for sample) procedure as a form of quality assurance/medico-legal requirement
Cranial Ultrasound	Maternal cocaine usePersistently abnormal CNS findingsSeizures
MRI	 Abnormal Cranial Ultrasound Seizures Persistently abnormal CNS findings
Blood/ Serum Glucose Calcium, Magnesium, Urea and electrolytes, FBC	- Excessive jitteriness or NAS-like presentation

Antenatal Management of Pregnancies/Foetus at Risk of NAS

Categories of Mothers/ Babies:

- 1. Mothers on prescribed medications likely to cause NAS/NAS-like features in babies
- 2. Mothers on Methadone Drug/ Alcohol Programme
- 3. Clinical concerns of possible NAS
- 4. Mothers with suspected illicit drug use, known to Social Services, with pre-birth care plan.

Consider the following management plan as appropriate (according to your local protocol):

- 1. Antenatal Counselling: for mothers in category 1&2 above, there should be a discussion between the mother, obstetrician and/or Senior Neonatal Team member on effects of such medication on the unborn and newborn baby.
- 2. Alerting the Neonatal Team
- 3. Involvement of the Midwifery Safeguarding Team/ Drug liaison midwife or team or anyone in a similar role (categories 2-4 above)
- 4. Multi-disciplinary antenatal plan (involving Social Services, Midwifery Safeguarding Team/ Drug liaison midwife or team /Midwifery staff, Obstetrician/ neonatal liaison, Health visitor (HV) and GP) in place for unborn baby and mother
- 5. Liaison with the Drug and Alcohol Services and Social services as appropriate
- 6. Smoking cessation counselling where appropriate

Delivery/perinatal Management

- > There is no requirement for neonatal team to be present for the delivery of a maternal drug misuse/use case unless there are other indications.
- Avoid the use of Naloxone in case of respiratory depression as this <u>may</u> precipitate an acute withdrawal and seizure (1 case report).
- Follow local protocol as appropriate.

^{*}Contact Details of local team should be made available - See Appendix 2



Postnatal Management

A. After delivery follow local protocol as indicated, including:

Information sharing, in selected cases as appropriate: informing neonatal team, social services, midwifery team with responsibility for safeguarding, Health Visitor (HV), Community Midwife (CM), Drug liaison midwife and GP (pre-discharge)

- Neonatal team to obtain the following information:
 - o Drug names, route, dose, frequency and duration
 - Timing of last dose
 - Details of any drug detoxification programme/ Drug and Alcohol Services, including the gestation at which it was started
 - Other drugs/ alcohol used
 - Drugs given to mother during labour
 - Family/ social history to include number of children living with parents/ foster care/ adopted or any social services involvement
 - Establish who has parental responsibility
 - o Booking and recent bloods including HIV, Hepatitis status of mother/ partner
 - Maternal history of mental illness and medication(s)
 - Record other problems during pregnancy and delivery

B. Initial Management:

- ➤ There should be a clear plan from the antenatal team, Social Services, Drug and Alcohol team, Safeguarding team or any other medical staff involved in or aware of concerns in the mother's notes.
- Documentation and any advice given to parents of babies who do not require any form of formal observation should be made in baby's notes/ or NIPE examination
- > Inform CM, HV and SS of baby's progress as appropriate
- > Observe as per local protocol on: NICU/SCBU/Postnatal ward/ Transitional care or as stated in the antenatal care plan
- ➤ Babies should only be separated from their mothers and admitted to NICU/SCBU if there are social, legal or medical reasons identified antenatally or for collection of urine (the urine collection needs to follow a chain of evidence pathway)
- The parents should be:
 - Involved in all care planning and delivery of care to their infant unless otherwise stated in pre-birth SS plan
 - Given every opportunity to discuss their baby's care and any concerns that they may have with the paediatrician and nursing staff
- Infants at risk of NAS or those whose mothers are suspected drug users should have the first withdrawal assessment using the Modified Finnegan Score(MFS), recorded at two hours of age (Appendix 1 for details and key points)
- Neonatal team should be made aware of any baby who starts exhibiting signs of withdrawal and admission to NICU should be considered (if scores are high and treatment is required).
- For babies whose mothers are on the Drug/ Methadone/ Alcohol Programme, known to misuse drugs, or in suspected cases of withdrawal and for those with antenatal plans to do so, some form of investigation may need to be carried out (see Table 5 above)



Admission Criteria

<u>Criteria for admission when baby is monitored on TC/PNW:</u>

- Baby is to be admitted to SCBU/NICU for monitoring and potential treatment if the score is ≥ 8 at any scoring interval
- Seizures
- Very unsettled, with continuous or intermittent high-pitched cry
- Poor feeding
- Other clinical concerns

Length of observation period when pharmacotherapy is not needed:

- Known Opioid-exposed infants should be observed for minimum 72 hours after birth, however the withdrawal symptoms might present as late as 14 days after birth
- Marijuana: No observation period required
- Cocaine: Babies may need to be monitored for cocaine effects for 48 hours
- > Poly-drug misuse: Minimum of 72 hours

Supportive/Non-Pharmacological Management

Regardless of the need for medication for the treatment of NAS, all drug-exposed infants should receive individualised non-pharmacologic supportive management, as NAS per se is not defined solely by the need for medication therapy. Initial management should primarily be supportive for symptom scores of less than 8. If, after the period of observation the baby is asymptomatic, he/she could be discharged home, provided that any possible social concerns have been addressed and resolved.

A. General Adjunctive Therapy:

Table 6: Adjunctive Therapy

Include:	
Soothing techniques	non-nutritive sucking using 'dummy'
	positioning/swaddling/ gentle movement/ rocking
Maintaining temperature stability	Appropriately clothed to avoid sweating
Minimal sensory stimulation	Do not disturb when asleep; minimal noise
Minimal Environmental stimulation	Dimmed lights/ use of developmental care principles
Frequent small feeding	3 hourly feeds
May require higher feed volume and/ or higher	This may be necessary to meet the high caloric requirements to ensure proper growth and should be



caloric formula	individualised
May have "sore bottoms"	Use (for example): Paraffin 50/50 , Medihoney barrier
	cream (or as per local protocol)

B. Nutritional Management:

- NAS infants may have a voracious appetite/ hyperphagia and hyperactive sucking action which can lead to excessive weight gain. Others may have poor suck coordination making it difficult to establish oral feeding and supplementary tube or cup feeding may be necessary
- Observe for signs of dehydration in case of persistent vomiting or loose stools and manage as appropriate
- Infants may be prone to weight loss and failure to thrive secondary to caloric expenditure caused by their hypermetabolic state or through vomiting, posseting and loose stools.
- > There is increasing evidence that using lactose free formula improves the stool consistency and perianal excoriation. This should be considered in formula fed infants.
- Breast feeding should be advocated as it may reduce the severity of withdrawal symptoms
- > If the baby is not to be breast-fed then frequent small volume feeding with hypercaloric formula to supply the additional caloric requirements may be needed
- Monitor weight at regular intervals according to local unit policy

C. Breast Feeding (BF):

BF has been shown to have several advantages including significantly reducing length of hospital stay, encouraging and improving bonding, lessening the severity of symptoms, reducing the duration of NAS and the need for withdrawal pharmacotherapy compared with formula-fed infants. The mother should be given all the necessary information to be able to make an informed choice

Table 7: Indications and Contraindications to BF

Indication	 Should be encouraged in mothers who are stable on methadone, however, advice to avoid breastfeeding within first 2hrs post-dose In mothers with concurrent hepatitis B or C, breastfeeding is not contraindicated (not known to be transmitted through BF) and especially if baby has been immunised
Relative contraindication	Mothers on high dose methadone
Contraindication	 HIV positive mothers Ongoing maternal cocaine, heroin, amphetamine use Known poly-drug misuse (or confirmed on urine toxicology in either the baby or the mother On IV Opiods CNS stimulants: Eg. Dexamphetamine, Methylphenidate



D. Parent Education:

It is important for the mother and family to understand the neuro-behaviour in their infant. They need to begin building skills to help their infant cope whilst still in hospital. Topics to discuss with mother include:

- Exaggerated rooting does not always indicate hunger
- Infants may be disturbed by normal household noises and may not sleep well
- Crying may be high-pitched
- > Hypertonia may persist and mother may interpret this as sign of rejection
- Drugs that pass through into the breast milk

C. Maternal Therapy:

Mothers who are not emotionally stable or not receiving appropriate medication and/or therapy are at high risk for relapse to drug use, neglect, or abuse of the child. The population of substance exposed infants and their caregivers is a complex and vulnerable group. Only through coordinated, comprehensive, and compassionate care can the difficulties created by in-utero substance exposure for the mother and the infant be overcome.

The following should form part of Maternal Management while baby is on the NICU:

- > Agreed social services plan should be followed if in place
- Ensure adequate drug-misuse therapy is on-going
- Effective communication strategies; parents should be given opportunities to discuss on-going care, honest feedback; frequent maternal-infant assessments. Reassurance and support are also important.
- Ensure on-going psychiatric care if required
- ➤ Encourage and supporting mother to care for the baby; it is important to prepare the mother to identify her feelings about an infant with NAS and to practice the emotional responses that will allow her to support the infant's recovery. Early experiences, such as positive caregiving during critical periods, can induce programming or reprogramming of key adaptive systems, such as stress response, that promote positive adaptation in young children that can result in healthier developmental, behavioural, and social-emotional trajectories
- Psychological care/ use of counsellors if available
- Offer rooming in pre-discharge
- Discuss follow-up plans pre-discharge

These techniques may be adequate treatment for some infants with NAS; however, pharmacological intervention is often necessary.



Pharmacological Management

Goals for initiating pharmacotherapy are to:

- 1. Ameliorate the clinical manifestations of withdrawal- hyperactivity and autonomic instability
- 2. Restore normal pattern of newborn activities, such as sleeping, feeding and consistent weight gain

<u>Criteria and Indications for starting pharmacological treatment include:</u>

- 1. Using MFS: the need for medication is indicated when:
 - ➤ The total score is 8 or higher for 3 consecutive scorings. Once the score is 8 or higher the scoring intervals automatically become 2 hourly, so significant symptoms are treated within 4-6 hours.
 - > Two consecutive scores of 12 or higher require therapy to be initiated. If the score is 12 or higher the baby must be assessed by 2 people individually.
 - ➤ When the sum of 3 consecutive Finnegan scores is > 24.
- 2. Seizures
- 3. Continuous high-pitched cry (see Appendix 1)
- 4. Inability to feed and rest (i.e. the infant sleeps less than one hour after feeds)
- 5. When there is profuse diarrhoea and frequent vomiting, poor feeding and poor weight gain (when other causes are ruled out), start treatment even if scores are < 8

Pharmacotherapy:

Numerous medications have been used to treat NAS including Benzodiazepines, Chloral hydrate, Chlorpromazine, Clonidine, Morphine, Methadone and Phenobarbital. However, there are very few quality RCTs and other less robust evidence to prove the superiority of one agent above the other. Current evidence point to the increasing trend in trials and use of Morphine and Clonidine, with decreasing use of other agents (Appendix 4: Trends in Current Pharmacotherapy used in NAS). Further evidence in support of this is provided in Appendix 5: Evidence Summary Table.

- > 1st line: Oral Morphine +/-
- 2nd line/ Adjunctive Therapy: <u>Clonidine or Phenobarbital</u> (*these have also been used as monotherapy in some trials and been compared to each other and to Morphine) (See Appendix 5: Evidence Summary Table)

Table 8: Medications, Dose and weaning process

	Drugs	Start, Increments, Maximum dose	Weaning Process	Dose at which to Stop
A.	1 st Line			
	Morphine			



	T : -	Г_	I	T
	Opiate Mu agonist Drug of choice for all opiate	Start: 50mcg/kg/dose orally Frequency:	1.Reduce dose by 10-20% every 24-48hrs	When total dose/day 125mcg/kg/day or less
	withdrawal 1 st line for seizures 2 ⁰ to	3-4hrly dose regime Increments:	if all scores <8 in preceding 24hrs until	Advantages: -Very effective in opiate-
	opiate withdrawal, polydrug	20%/dose *Max dose:	reaching starting dose of	related NAS
	misuse Monitor: 4-	1000mcg/kg/day (167mcg/kg 4hrly)	50mcg/kg/dose 3-4hrly	Disadvantage: -Respiratory depression
	6hrly Respiratory rate	* Units using a max daily dose of <400 mcg/kg/day were more likely to	2. Then decrease frequency:	-Sedation -Frequent dosing
	Heart rate Blood pressure	require the addition of 2 nd line Rx (O'Grady et al)	from 4 to 6 to 8 to 12 hourly	
	pressure			
B.	2 nd Line	Indications for starting: 1. When close to or at maxi 2. Poly-drug use 3. To shorten duration of M 4. To help reduce persisten	ose	
		5. Found to help reduce the		e required
1.	Clonidine:			
	Centrally	Start:	Weaning:	Stop:
	Centrally acting α ₂ -	Start: 6mcg/kg/day orally	Weaning: Wean off	Stop: 1.5mcg/kg/day or less
				•
	acting α ₂ - adrenegic agonist	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure	Wean off Morphine first	1.5mcg/kg/day or less Advantages:
	acting α ₂ - adrenegic agonist Monitor:	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the	Wean off Morphine first Start weaning	1.5mcg/kg/day or less Advantages: -Quicker wean
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4-	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure	Wean off Morphine first Start weaning after 48hrs off	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose)	Wean off Morphine first Start weaning	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting,	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency:	Wean off Morphine first Start weaning after 48hrs off Morphine	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose)	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required,
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime	Wean off Morphine first Start weaning after 48hrs off Morphine	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments:	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when weaning till	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments: 25% Max: 12mcg/kg/day	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to Phenobarbital -No sedative effect -No respiratory
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when weaning till 24hrs after	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments: 25% Max: 12mcg/kg/day Clonidine may not be	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to Phenobarbital -No sedative effect
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when weaning till 24hrs after	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments: 25% Max: 12mcg/kg/day Clonidine may not be readily available as it is	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to Phenobarbital -No sedative effect -No respiratory depression
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when weaning till 24hrs after	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments: 25% Max: 12mcg/kg/day Clonidine may not be readily available as it is an unlicensed special	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to Phenobarbital -No sedative effect -No respiratory depression Disadvantages:
	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when weaning till 24hrs after	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments: 25% Max: 12mcg/kg/day Clonidine may not be readily available as it is	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to Phenobarbital -No sedative effect -No respiratory depression Disadvantages: Frequent BP, HR
2	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when weaning till 24hrs after stopping	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments: 25% Max: 12mcg/kg/day Clonidine may not be readily available as it is an unlicensed special	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to Phenobarbital -No sedative effect -No respiratory depression Disadvantages:
2.	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when weaning till 24hrs after stopping	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments: 25% Max: 12mcg/kg/day Clonidine may not be readily available as it is an unlicensed special drug	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to Phenobarbital -No sedative effect -No respiratory depression Disadvantages: Frequent BP, HR
2.	acting α ₂ - adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when weaning till 24hrs after stopping	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments: 25% Max: 12mcg/kg/day Clonidine may not be readily available as it is an unlicensed special drug Start options:	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by	1.5mcg/kg/day or less Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to Phenobarbital -No sedative effect -No respiratory depression Disadvantages: Frequent BP, HR
2.	acting α₂- adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when weaning till 24hrs after stopping Phenobarbital Barbiturate	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments: 25% Max: 12mcg/kg/day Clonidine may not be readily available as it is an unlicensed special drug	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by 10% 24hrly	Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to Phenobarbital -No sedative effect -No respiratory depression Disadvantages: Frequent BP, HR monitoring
2.	acting α₂- adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when weaning till 24hrs after stopping Phenobarbital Barbiturate Decreases	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments: 25% Max: 12mcg/kg/day Clonidine may not be readily available as it is an unlicensed special drug Start options: 1. Loading dose (*may help achieve therapeutic levels quicker):	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by 10% 24hrly Wean off	Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to Phenobarbital -No sedative effect -No respiratory depression Disadvantages: Frequent BP, HR monitoring Wean Phenobarbital over
2.	acting α₂- adrenegic agonist Monitor: BP and HR 4- 6hrly for 48hrs after starting, then 12hrly and back to 6hrly when weaning till 24hrs after stopping Phenobarbital Barbiturate Decreases hyperactivity	6mcg/kg/day orally (give 1mcg/kg then assess blood pressure before increasing the dose) Frequency: 4-6hly dose regime Increments: 25% Max: 12mcg/kg/day Clonidine may not be readily available as it is an unlicensed special drug Start options: 1. Loading dose (*may help achieve therapeutic	Wean off Morphine first Start weaning after 48hrs off Morphine Decreased by 10% 24hrly Wean off	Advantages: -Quicker wean -In combination with Morphine, reduces MFS quicker, reduces total Morphine dose required, shortens length of stay -Shorter therapy time compared to Phenobarbital -No sedative effect -No respiratory depression Disadvantages: Frequent BP, HR monitoring Wean Phenobarbital over



Sedative-	10/mg/kg/day, to be given	-In combination with
Hypnotic	in 2-3 divided doses (8-	Morphine, reduces FS
withdrawal	12hourly) orally	quicker, reduces total
		Morphine dose required,
Monitor:		shortens length of stay
Periodic	2. No loading dose	
Phenobarbital	regime: 5-10/mg/kg/day,	Disadvantage:
levels	to be given in 2-3 divided	-Over sedation
Keep levels	doses (8-12hourly) orally	-Needs levels monitoring
20-30mg/l		-Overall longer therapy
_	Frequency:	time compared to
	12hrly dose regime	Clonidine
		-Need for outpatient
	Max: 10-12mg/kg/day	follow up and weaning
	orally	-? Potential adverse
		effect of Phenobarbital on
		developing brain

Care coordinator for the baby on the NICU

- There will be close liaison between the Neonatal Team, the Midwifery Safeguarding Team, Social Services/ Social Worker, any identified keyworker, Drug liaison midwife, the Health Visitor and the GP.
- On the NICU, this will be coordinated and facilitated by a named team member, eg. Neonatal Community Nursing Team with regular updates of progress.

Discharge on home medication

Some babies (e.g. babies discharged to foster care, babies born to mothers on prescribed opioids for pain management) may be discharged home on medication, once symptom control has been achieved:

- Morphine (weaning can follow the above regime)
- Phenobarbital can be weaned within 3 months

Discharge Planning

- ➤ All routine discharge procedures must be followed.
- ➤ NAS babies should have been off medications for at least 24-48hrs with NAS Scores of less than 8 before discharge.
- Exception to above is the use of Phenobarbital. Administration competency should be achieved by parents/foster carer before discharge.

In addition:

- The Neonatal Community Nursing Team will facilitate and coordinate the discharge of the babies who required treatment, in liaison with the appropriate professionals including the GP, Health Visitor, Social Worker, Midwifery Safeguarding Team, the social worker and Drug/ Alcohol Rehabilitation Team
- A discharge planning meeting should be held, where considered necessary, with parents/ family/ Foster carer (as applicable), Health Visitor, Social worker with



typed copy of the minutes to be included in the clinical notes. Local services such as Drug/Alcohol Rehab Team should also be informed. This is to allow the key workers adequate time to organise and co-ordinate post discharge substance use review and care i.e. medication, methadone / other prescribed medication (if applicable), appointment with the doctor / key worker etc.

- ➤ Complete a 'SEND' discharge summary with details of the HV, SW for GP with copies to social worker (as applicable), health visitor and the family. Care must be taken not to include any sensitive information.
- For Babies going into Foster Care, a special discharge form or letter should be devised to be given to Foster carers with detailed ongoing care or follow up plan

Follow up

- For infants discharged on Phenobarbital, there should be a weaning protocol aimed at stopping the medication within the first 3 months of age
- Arrange Paediatric/ Neonatal Consultant follow up for all the symptomatic babies who required treatment
- For babies who are discharged to Foster Care, referral to 'Looked After Children's Medical team (part of the Community Paediatric Team) for subsequent follow up should be arranged.
- It is recommended (American Association of Paediatrics guideline) for babies diagnosed with NAS, who required pharmacological treatment, to have neurodevelopmental assessment at 2yrs

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Appendix 1: Finnegan Scoring System

The <u>most widely validated</u> of the NAS Scoring Tools is the **Finnegan Scoring Tool**. The **Finnegan Scoring Tool** NAS score sheet lists 21 symptoms that are most frequently observed in opiate exposed babies. Each symptom and its associated degree of severity are assigned a score and the total abstinence score is determined by totalling the scores assigned to each symptom over the scoring period.

KEY POINTS

- The first score should be recorded either 2 hours after birth or admission to the nursery to give a baseline score.
- Following that baseline score all babies should be scored at 4 hourly intervals, except when high scores indicate more frequent scoring.
- A new sheet should be started for each day.
- Scoring is dynamic. All signs and symptoms observed during the scoring interval are included in the points total for that period.
- If the baby is scoring 8 or more at any interval scoring should be increased to 2 hourly and continued for 24 hours from the last score of 8 or higher.
- If the baby scores 7 or less for a 24 hour period, 4 hourly scoring may be resumed.
- If no treatment is required the baby should be scored for the first 4 days of life at 4 hourly intervals.



- If treatment required the baby should be scored at 2 or 4 hourly intervals dependent on scores.
- Once treatment has been stopped continue scoring for 48 hours then stop.

GUIDE TO ASSSESSMENT AND SCORING

The scoring system was designed for term babies on 4 hourly feeds and may need modification for a premature baby.

In term babies scoring should be performed 30 mins-1 hour after a feed, before the baby falls asleep

If the baby is woken to be scored then diminished sleep after scoring should not be recorded. A crying baby should be soothed and quietened before assessing muscle tone, Moro and respiratory rate.

GUIDE TO ASSSESSMENT AND SCORING:

High pitched cry	Score 2 if high pitched at its peak Score 3 if high pitched throughout Baby is scored if crying is prolonged even if it is not high pitched
Sleep	A premature baby on 3 hourly feeds can sleep for 2.5 hours at most. Score 1 if less than 2 hours Score 2 if less than 1 hour Score 3 if no sleep between feeds
Moro reflex	Score if the baby exhibits pronounced jitteriness of the hands during or at the end of a Moro reflex. Score 3 if jitteriness of hands and arms present during or after initiation of the reflex.
Tremors	This is a scale of increasing severity. Only one score should be used from the 4 levels of severity. Undisturbed refers to the baby asleep or at rest in the cot.
Increased muscle tone	Score if above normal muscle tone/tension is observed. Muscle tone becomes stiff/rigid, the baby does not experience any head lag when pulled into a sitting position.
Excoriation	Abrasions resulting from rubbing against a surface covered in fabric. Score only when excoriations 1 st appear, when they increase/worsen, or appear in a new area.
Myclonic jerks	Score if involuntary muscular contractions which are irregular and abrupt are observed.
Generalised convulsions	Unusual limb movements may accompany a seizure. In the upper limbs these often resemble "swimming" or "rowing". In the lower limbs they resemble "pedalling" or "bicycling. Other signs may include eye staring, rapid involuntary eye movements, chewing, back arching and fist clenching.
Sweating	Score if sweating is not due to excessive clothing or high room temperature
Hyperthermia	Temperature should be taken per axilla. Mild pyrexia (37.2 – 38.3) is an early indication of heat produced by increased muscle tone/tremors.
Yawning	Score if more than 3 yawns observed within the scoring interval.
Mottling	Score if mottling is present on the baby's chest/trunk/arms/legs.
Nasal stuffiness	Score if the baby sounds congested, mucous may/may not be visible.
Sneezing	Score if more than 3 sneezes observed within the scoring interval.
Nasal flaring	Score only if repeated dilation of the nostrils is observed without other evidence of lung/airway disease.
Respiratory rate	Score only if >60 per minute without other evidence of lung/airway disease Score 2 if respirations involve intercostal retractions.
Excessive sucking	Score if hyperactive/disorganised sucking, rooting or attempts to suck fists/thumbs (more than an average hungry baby) are observed.



Poor feeding	Score if the infant demonstrates excessive sucking prior to a feed yet sucks infrequently during the feed taking a small amount and/or demonstrates an uncoordinated sucking reflex. Premature infants may require tube feeding and should not be scored for poor feeding if tube feeding is to be expected at their gestation.
Regurgitation	Score if at least 1 episode is observed, even if contained in the mouth.
Loose watery stools	Score if loose (curdy/seedy) Score if watery (water ring on nappy around stool)

Neonatal Abstinence Scoring System

	SIGNS SYMPTOMS	SCOR E	Α	M			Р	M	COMMENTS
	DATE/TIME								
s	Excessive high pitched (or other) cry <5mins Continuous high pitched (or other) cry >5mins	3							
ymptom	Sleeps <1hr after feed Sleeps <2hrs after feed Sleeps <3hrs after feed	3 2 1							
tem s	Hyperactive Moro Reflex Markedly hyperactive Moro Reflex	2 3							
Central Nervous System symptoms	Mild tremors when disturbed Moderate-severe tremors when disturbed Mild tremors when undisturbed Moderate-severe tremors when undisturbed	1 2 3 4							
a N	Increased muscle tone	1							
entr	Excoriation	1							
ŭ	Myclonic Jerks (twitching jerking of limbs)	3							
	Generalised convulsions	5							
>	Sweating	1							
Metabolic/Vasomotor/Respiratory symptoms	Hyperthermia 37.2-38.3 Hyperthermia >38.4	1 2							
r/Res	Frequent yawning (>3-4 times/scoring interval)	1							
asomotor/F symptoms	Mottling	1							
som/	Nasal Stuffiness	1							
/Va	Sneezing (>3-4 times/scoring interval)	1							
olic	Nasal Flaring	2							
Metab	Respiratory rate >60/min Respiratory rate >60/min (with retractions)	1 2							
	Excessive sucking	1							
smo	Poor feeding or excessive feeding	2							
GIT Symptoms	Regurgitation (≥ 2 times during /post feed Projectile vomiting	2 3							
GIT 8	Loose stools Watery stools	2 3							
	TOTAL SCORE								
	INITIALS OF SCORER								



The scores should be charted for the symptoms seen during the interval between the last scoring and present scoring, not necessarily at the time of recording.

The need for medication is indicated when the total score is 8 or higher for 3 consecutive scorings.

Once the score is 8 or higher, the scoring intervals automatically become 2 hourly, so significant symptoms are treated within 4-6 hours.

If the score is 12 or higher, the baby must be assessed by 2 people individually.

2 consecutive scores of 12 or higher requires therapy to be initiated at the appropriate dosage

Reference: Adapted from- Neonatal Abstinence Score from Finnagan LP (1986), Neonatal Abstinence Syndrome: Assessment and Pharmacology

Appendix 2: Important Contact Details (Sample)

Neonatal Intensive Care Unit	Ext:
High Dependency/ Special Care Baby	Ext:
Unit	
Neonatal Nursing Team Responsible	Bleep:
for Drug Misuse and Alcohol	Ext:
Named Responsible Neonatal	Neonatal Secretaries:
Consultant	Ext:
Neonatal Consultant on-call	Bleep
	Ext:
Neonatal Sister-in-charge	Bleep:
	Ext:
Midwifery Team with responsibility for	Bleep:
Drug and Alcohol Misuse	Ext:
Local Social Services Team	
Local Drug and Alcohol	Tel:
Services/Treatment Team	
Other staff contact as required	Tel:
	Bleep:



Appendix 3: Chain of Custody Form: Urine Toxicology (Sample)

Hospital Logo	Patient label/ Details	
		ر

CHAIN OF CUSTODY FORM

Department of Pathology

Sample Accession Number:

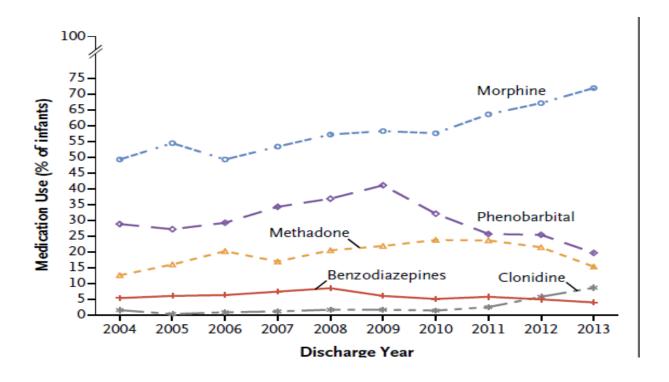
Date	Time	Name of person handling sample	Action taken	Signature
		Nurse:	Sample taken	
		Porter:	Sample sent to lab	
		Lab reception:	Sample received Accession number allocated	
		Lab technician:	Sample analysed	
		Etc		

^{**}The form should accompany the sample until after analysis of the sample and results put in the patients lab results system



Appendix 4: Trends in current pharmacotherapy used in NAS management Increasing use in Morphine and Clonidine, with decreasing use in all other agents

(Tolia V, Patrick S, Bennett M, et al. Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. N Engl J Med. 2015;372:2118-2126)





Appendix 5: Evidence Summary: Trials/ Case Series using/comparing Morphine, Clonidine & Phenobarbital

	Study/Trial/Case series (All term or near term infants)	Medication & Dose	Weaning Protocol	Minimum dose at which it was stopped
1	Surran et al 2013, J Perinatology Non-blinded RCT Opiate exposed infants 34 infants in each arm Grp 1: M+Clonidine OR Grp 2: Phenobarbital MFS >8 x2 3hr apart Opiate exposure + poly drug use BP 6hly for 48hr then 12hrly; back to 6hly when on Clon alone till 24hrs after coming off	Morphine: Start 320mcg/kg/day = 40mcg/kg 3hrly Max 800mcg/kg/day = 100mcg/kg 3hly + Phenobarbital: Start 6mg/kg/day Max 12mg/kg/day 8hrly doses Versus Clonidine: Start 6mcg/kg/day 6hly dosing Max 12mcg/kg/day	Weaned Morphine first Reduce dose by 10% every 24hrs if all scores <8 in preceding 24hrs Phenobarbital Weaning schedule after discharge Clonidine Started weaning 24hrs after stopping Morphine ½ the dose every 24hrs and stop at 1.5mcg/kg/day	Phenobarbital Stopped at home Clonidine 1.5mcg/kg/day Results: Both study grps showed Shorter duration of stay compared to pre-trial Morphine monotherapy. Phenobarbital compared with Clonidine had shorter Morphine Rx days with no difference in average Morphine total dose (therefore comparable efficacy in NAS Rx). Post-discharge, Phenobarbital was continued for an average of 3.8 months. 2pts in Clonidine group failed weaning 7 successfully Rx on Phenobarbital 3 pts in Phenobarbital grp showed signs of over sedation No CVS adverse effects in
				Clonidine group
2	Bada et al, 2015; Pediatric Pilot Prosp double-blind RCT 15 and 16 pts in each arm respectively Known prenatal opiate exposure Morphine monotherapy OR Clonidine monotherapy Urine toxicology only opiate and few Benzodiazepine	Morphine: Start: 400mcg/kg/day in 3hlry doses= 50mcg/kg/dose 25% increase/day Max 1000mcg/kg/day = 125mcg/kg 3hly Clonidine: Start: 5mcg/kg/day 3hly = 0.625mcg/kg	Morphine: Weaned Morphine first, 10% dose reduction 48hly Clonidine: 10% dose reduction 48hly	Morphine: When dose <100mcg/kg/day Clonidine: When dose <1mcg/kg/day Results: Rx duration was significantly longer for Morphine than Clon Neuro-behavioural scores
3	MFS >8 x3 3hrs apart or >12 x2 Addition of 2 nd drug when max daily doses reached BP monitoring Agthe et al, 2009 Pediatrics	Max 12mcg/kg/day 1.5mcg/kg 3hly		(NNNS) improved significantly with Clonidine but not with Morphine. On subsequent assessment, those receiving Clonidine had lower height of arousal and excitability. No infant in the study required a 2 nd medication
		Morphine:	Weaned Morphine	Not clear



				(Hostea by Cambriage University Hospitals)
	Double blind RCT Exposure to Methadone or Heroin 40 pts in each arm Morphine+Clonidine OR Morphine+Placebo 1º outcome = Duration of M therapy Used MFS of ≥9 on 2 occasions BP, HR monitoring	Start: 200mcg 4hrly Increment: 100mcg/dose Max dose: 900mcg 3hrly Clonidine: Start: 1mcg/kg/4hly = 6mcg/kg/day Increment till Max 12mcg/kg/day	first Start after 48hrs of control; decreased by @ 14% 24hrly	Results: Shorter duration of Rx and lower total dose for Morphine+Clonidine group. 5 Rx failure in the Morphine+Placebo group, none in M+C grp. HR and BP lower in Clonidine group but within normal range
4	Esmaeili et al, 2010, Acta Paed. Retrospective Review Exposure: Mothers on Methadone Program Comparing combination Rx of: Clonidine+/-Chloral Hydrate (29pts; PICU setting) Vs Morphine+/-Phenobarbital (64 pts) 2nd agent, i.e., chloral and Phenobarbital is only added when max dose of 1st agent Clonidine or Morphine is reached Used MFS >10 x1 BP monitoring	Clonidine: IV infusion Start 12mcg/kg/day Max 72mcg/kg/day +/- Chloral Hydrate: 30-50mg/kg/dose max TDS Morphine: Start 300mcg/kg/day Max 800mcg/kg/day +/- Phenobarbital BD dosage 20mg/kg/day 1st day 5mg/kg/d from 2nd day Max 10mg/k/day	Stepwise increase, rate not stated	Stop: Not stated Results: Rx duration significantly shorter in clonidine/chloral hydrate group & group also exhibited markedly reduced withdrawal symptoms. BP was comparable in the 2 groups
5	Double blind RCT on Rx for NAS Exposure: Opiates and other drugs Morphine (41 pts) Vs Phenobarbital (34 pts) Used Lipsitz tool for scoring	Start: Morphine 50mcg/kg QDS Vs Phenobarbital 2mg/kg QDS (no loading dose**) Increments: 20% increase in dose Adjunct Medication: Chloral Hydrate 15mg/kg ** Kaltenbach & Finnegan compared 36 drug exposed infants treated with Phenobarbital regimens that did or did not use a loading dose. No significant difference was identified between regimens	Wean: 20% decrease in dose every 48hrs (not the decrease in frequency)	Results: Morphine grp required fewer days active Rx. Maternal methadone dose independently influenced the duration of Rx Infants receiving Phenobarbital grp tended to require an additional drug more often Other factors also appeared to correlate with the requirement for second line Rx, including: maternal methadone dose, in utero exposure to classes of drugs other than opiates or benzodiazepines, and exposure to benzodiazepines



e	Covide et al. 2002 I De d			
6	Coyle et al. 2002, J Ped,	Start:	Wean:	Stop:
	Partially RCT 20 cases, 10 each arm	Morphine 50mcg/kg/dose 3-	Morphine by 0.1ml if FS<5 8hrly x3	Not clear
	FS >7	4hrly (0.4mg/ml) Increments::		Results:
	Combination of Morphine+Phenobarbital	0.1ml = 125mcg		The duration of stay was reduced by 48% for the
	Morphine alone Monitored: ECG, HR, electrolytes and Clonidine levels	Phenobarbital Loading 10mg/kg 12hrly x3 Maintenance 2.5mg/kg BD to achieve blood levels of 20-30mg/dl (previously been shown to control NAS symptoms in 94% of patients)	Phenobarbital: weaned by GP over 2-9 mon	Morphine and Phenobarbital group; these infants spent less time with severe withdrawal, and required a lower max daily Morphine dose when compared with the Morphine-only group. The mean duration of outpatient Phenobarbital use was 3.5 months.
7	Kandall D et al Am J Dis Child.			
	1983	Start: Morphine:	Weaning:	Stop: Not stated
	RCT	80mcg/kg 3hrly	Starts 5 days after symptom control	Not stated
	Morphine (49 pts)	la a rama anti	By 20mcg/kg/dose	Decultor
	Vs	Increment: 20mcg/dose		Results: Both Morphine and
	Phenobarbital (62 pts)	-		Phenobarbital controlled
	42 randomised pts did not require any Rx	Max not given		symptoms equally well; 7/62 Phenobarbital treated newborns had abstinence-associated
	Exposure: maternal opiate and ½ in each grp abused other drugs	Phenobarbital: 5mg/kg/day in 8hrly doses		seizures within the first month of life, 42 neonates initially requiring no Rx were born to mothers taking less methadone just before delivery, however 5/42 had seizures within the first 14 days of life
	Used Lipsitz scoring system	Increment: 1mg/kg/day until symptom control Max not given		
8	Hoder et al. N Engl J Med.1981	Both case series	25% decrease in total	Stopping dose not started:
	and Hoder <i>et al</i> . Psychiatry Res.	started Clonidine at:	dose every 48hrs	Minimum dose used was
	1984	0.5-1mcg/kg 4-6hrly Titrated up towards		0.5mcg/kg 6hrly
	2 Separate Case series	maintenance dose of		
	Both used Clonidine	3-5mcg/kg/day in 4- 6hrly doses		Results: Achieved Rx in 6/7 in each case
	monotherapy	5, dood		series at highest maintenance
	7 infants in each case series			dose The 2 failed Rx had been
	were exposed to maternal			exposed to Haloperidol,
	Methadone			Desipramine and Theophylline. Mean length of Rx 13 in one
	Used Finnegan Scoring system			case series and 12.2 days in the other (ranges 6-27 and 6-17 days) Clonidine levels did not correlate with symptom control No adverse effects were noted



Appendix 6: Audit of Practice

A list of all Babies admitted to the Neonatal Unit/ Transitional Care for NAS management and for Urine Toxicology sample taken, should be kept by the Neonatal Team

Auditing Tool/ Proforma (Sample)

Hospital Number	
Date of birth	
Social Services involvement	Yes[] No[]
Antenatal plan in place	Yes[] No[]
Maternal details	
Patient label	Age: Occupation: Ethnicity: Parity: Marital status: Mental health issues: Yes [] No [] Received antenatal care: Yes [] No [] Alcohol Use: Smoking: Yes [] No [] Number/day: Serology: HIV (Y/N) Hep B (Y/N) Hep C (Y/N)
Reason for admission	
Known maternal drug misuse	Name of Drug(s):
If on Methadone programme- Daily dose	<u> </u>
Suspected maternal drug misuse/ Suspected NAS in infant And Mathadana programma. Daily dasa.	Name of Drug(s)
If on Methadone programme- Daily dose 3. Maternal medication	
Baby	
Patient label	Gestational Age: Gender: Weight: Centile: Head Circumference: Centile:
Date & Day of admission	
Date & Day of discharge	
Total number of Days on the Unit	
Date, time & Day Urine Sample obtained	
Was mother given an opioid perinatally	Yes [] No []
during labour?	If Yes, name:
Urine Toxicology results with Dates	Date of Formal report:
	Report:



Date & Day of life Starting Morphine	
Maximum Dose of Morphine required	
Maximum score(s)	
Date and Day of life of above	
Date & Day of stopping Morphine	
Total number of days on Morphine	
Was 2 nd agent required	Yes [] No []
Name of 2 nd agent used	res[] No[]
Maximum dose of 2 nd agent	
Date & Day of starting 2 nd agent	
Date & Day of stopping 2 nd agent	
Treatment failure (change in 2 nd agent;	Yes [] No []
symptom rebound after stopping all	Change from:to
medication)	Ghange from:
Any Adverse effect from Medication	Yes [] No []
7 m.y 7 m. c.	If yes, please list:
	you, product not
Discharge Planning meeting held	Yes [] No []
Feeding type	Breast feeding [] Bottle []
5 71	Expressed Breast milk []
	High energy formula required?
	Yes[] No[]
Discharge	Date:
	Day of Life:
	Discharged on medication: Yes [] No []
	Name of medication:
Discharged route:	
	Home to Parents []
	Family member []
	Foster care []
Comorbidity/ties during stay: List	1.
	2.
	3.
Follow up arranged	Yes [] No []
If infant went home on medication, age at	Date:
which it was stopped	Age:
2yr Neurodevelopmental outcome	



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Form to be completed in the **exceptional** circumstances that the Trust is not able to follow ODN approved guidelines.

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Surname:	Telephone contact number:				
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Rationale why Trust is unable to adhere to the document:					
Signature of speciality Clinical L	ead: Signature of Trust Nursing / Medical Director:				
Date:	Date:				
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