

Neonatal abstinence syndrome: the role of breastfeeding

Treatment for neonatal abstinence syndrome (NAS) can be prolonged, in some cases necessitating a lengthy hospital stay. There is increasing evidence that breastfeeding affected infants can be beneficial in reducing the severity and intensity of symptoms of NAS. Substance misusing mothers are a vulnerable group with low breastfeeding rates. Support and a positive attitude from healthcare professionals are essential in helping these women to breastfeed their infants. This review, based on current literature and local experience from a tertiary care unit, evaluates breastfeeding in infants susceptible to NAS and suggests strategies to promote breastfeeding among this group of women.

Munisha Balain

MBBS, MRCPCH
Specialty Registrar, Embrace, Yorkshire and Humber Infant and Children's Transport Service, Barnsley
munisha.balain@nhs.net

Kathryn Johnson

MBChB, FRCPC
Consultant Neonatologist, Neonatal Unit, Leeds General Infirmary

Keywords

substance misuse in pregnancy; neonatal abstinence syndrome; breastfeeding

Key points

Balain M., Johnson K. Neonatal abstinence syndrome: the role of breastfeeding. *Infant* 2014; 10(1): 9-13.

1. Neonatal abstinence syndrome (NAS) is a common problem on postnatal wards and neonatal units
2. Breastfeeding reduces the severity and intensity of symptoms of NAS thus reducing the need for treatment and the length of hospital stay.
3. Information provision and education of healthcare professionals about the benefits of breastfeeding in NAS may help to improve breastfeeding rates and reduce the burden of disease.

Substance misuse within the UK population continues to be a major public health concern (**FIGURE 1**)¹. Approximately one in four of those entering drug treatment programmes in 2010-2011 were female, many of who were of childbearing age. Pregnant substance misusing women need supportive and coordinated care during pregnancy. They have been highlighted as a specific group in need by the National Institute for Health and Care Excellence (NICE) in their guidance on the management of pregnant women with complex social factors².

Locally in Leeds, between 50 and 80 pregnant drug users book for antenatal care at the Leeds Addiction Unit (LAU) every year. The numbers have remained relatively static over a five-year period (**FIGURE 2**). The vast majority of these women are receiving prescribed opioid maintenance therapy (ie methadone or buprenorphine) with many using additional illicit substances. Infants born to substance misusing mothers are at a higher risk of poor pregnancy outcomes including prematurity, intrauterine growth restriction and stillbirth^{3,4}.

NAS: the effect of maternal substance misuse on the newborn infant

The sudden cessation at birth of a continuous supply of an addictive substance (most often an opioid) via the

placenta can lead to the development of NAS in the days after birth. NAS is characterised by a variety of symptoms, which are unpleasant for the infant and can be difficult to treat. The common clinical features of NAS are detailed in **TABLE 1**.

Up to 80% of drug-exposed infants develop NAS⁵ with many requiring pharmacological treatment, often necessitating a prolonged stay within the neonatal service⁶. Over the last decade, evidence from the literature consistently supports the use of morphine as the treatment of choice in infants where pharmacological treatment is necessary^{5,7,8}.

In addition to opiate treatment, non-pharmacological supportive care of these infants is vital. A recent report from the American Academy of Paediatrics highlights the need for non-pharmacological supportive measures, eg minimising environmental stimuli⁹; simple techniques such as nursing in a quiet room with dim lighting may offer significant benefit¹⁰.

Evidence in support of breastfeeding in the management of NAS

Breastfeeding rates in mothers whose infants are at risk of NAS are lower than that of the general population¹¹. There is evidence however, that breastfeeding may be a strategy that can be used to manage, treat or even prevent NAS.

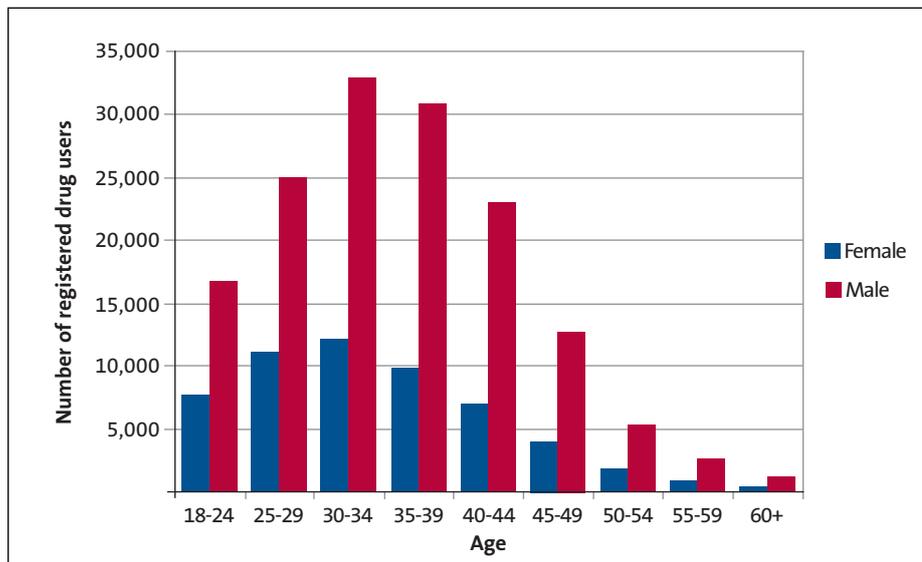


FIGURE 1 Age and gender of UK drug users registered for treatment in 2010-11¹.

Respiratory	Neurological	Gastrointestinal dysfunction	Autonomic signs
Tachypnoea	Tremors Irritability Hypertonicity Seizures	Poor feeding Poor weight gain Vomiting Diarrhoea	Sweating Nasal stuffiness Fever Mottling

TABLE 1 Common clinical features of neonatal abstinence syndrome.

In order to study the link between breastfeeding and NAS, a literature review was conducted with the following PICO question¹²:

In infants born to drug-dependent mothers (Patient), does breastfeeding (Intervention), as compared to formula feeding (Comparison), lead to reduced NAS symptoms (Outcome)?

Seven relevant studies were found, the results of which are summarised in TABLE 2. In summary, the studies consistently show that breastfed infants born to substance misusing mothers have significantly less symptoms of NAS, need less treatment for NAS and have a shorter duration of hospital stay compared to formula fed infants. These effects are seen regardless of the length of gestation and the type of drug exposure. However, there are a number of limitations to these studies:

1. The studies are often difficult to conduct due to the inherent nature of the topic studied – most instances rely on self-disclosure as a means of identifying drug use.
2. Feeds are often mixed (ie both formula and breast milk) leading to difficulty in analysis of results.
3. The breastfed and formula fed groups are self-selected and it is difficult to

match groups and establish stringent controls.

4. In many of the studies, the mothers in the formula fed cohort were younger, more likely to be unemployed, had less antenatal visits, comprised more polydrug users and belonged to a more socially disadvantaged group¹³.
5. Conversely, breastfeeding mothers were more likely to have comprehensive antenatal care, less likely to admit to polydrug use and were less likely to be notified as an at-risk parent to the child welfare services.
6. Formula fed infants are generally from higher risk groups, possibly confounding the results.

Despite the limitations, the strength of the evidence appears in favour of a positive effect of breastfeeding in infants with NAS.

Why do breastfed infants have fewer symptoms than formula fed infants?

One logical explanation is that opioids are excreted in breast milk, leading to an infant's continued exposure to the drug and hence less withdrawal symptoms. There have been a number of studies, particularly in relation to methadone, aiming to quantify the amount of

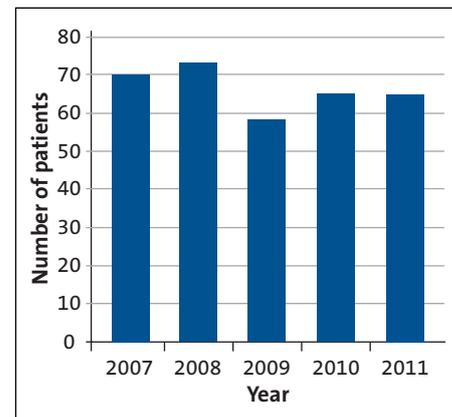


FIGURE 2 Number of drug-using women booking at Leeds Addiction Unit antenatal clinic.

methadone excreted in breast milk. These studies have unequivocally concluded that only low levels of methadone are excreted into breast milk (TABLE 3).

Many authors have suggested that the levels of methadone transmitted in human milk are below the threshold of physiological significance. The question is, are there other factors, instead of or in addition to, passive transference of opioids in breast milk that lead to the mitigating effects of breastfeeding in NAS?

Supportive care measures such as soothing, swaddling and frequent feeding are known to alleviate the symptoms of NAS. It has been shown that caring for infants with NAS on the postnatal ward with their mothers rather than on the neonatal unit reduces the need for treatment and duration of hospital stay, even when breastfeeding is not a factor²⁶. Breastfeeding is associated with an increased one-to-one time and interaction between mother and infant. Therefore some beneficial effects of breastfeeding could be related to the positive effects of mother-child bonding and one-to-one care of the withdrawing infant, rather than the components of breast milk²⁷.

However, the comforting effects of the act of breastfeeding do not entirely explain the differences between breast and formula fed infants in NAS. The benefits of breast milk have also been seen in infants who are fed maternal breast milk by gavage tubes, without the comfort of sucking¹³. These benefits are also seen when expressed breast milk is given to premature infants with NAS¹³. In addition, rebound withdrawal symptoms requiring pharmacological treatment following abrupt cessation of breastfeeding have also been described²⁸ and this finding is

Citation	Study type (S) Study group (G)	Key results
Abdel-Latif et al ¹³	S: Retrospective cohort study G: 190 drug-dependent mother and infant pairs	Mean withdrawal scores for breastfed infants were significantly less than formula fed infants. Breastfed infants were significantly less likely to require treatment for withdrawal and when treatment was needed, maximum morphine doses were less. Mean duration of hospitalisation for formula group was five days longer than breastfed group.
Jansson et al ¹⁴	S: Matched case-control study G: Eight methadone-maintained lactating mother and infant pairs, eight matched formula-fed subject pairs	Fewer infants in the breastfed group required treatment for NAS.
Dryden et al ³	S: Retrospective cohort study G: 450 singleton infants born to drug misusing mothers	Breastfeeding ≥ 72 hours was associated with halving the odds of requiring treatment for NAS.
Isemann et al ¹⁵	S: Retrospective cohort study G: 142 infants who received opioid therapy for NAS	Maternal breastfeeding was associated with a shorter duration of treatment and hospital stay in both preterm and term infants.
McQueen et al ¹⁶	S: Retrospective cohort study G: 124 women in opioid maintenance treatment in pregnancy	Breastfeeding is associated with shorter duration of symptoms and less pharmacological treatment.
Pritham et al ¹⁷	S: Retrospective descriptive study G: 152 opioid-dependent pregnant women and their neonates	Breastfed infants were discharged home earlier than those who were formula fed.
Welle-Strand ¹⁸	S: Retrospective and prospective cohort study G: 124 women in opioid maintenance treatment during pregnancy and their neonates	Breastfed neonates had a significantly lower incidence of NAS. Breastfed neonates had a shorter duration of pharmacological treatment for NAS.

TABLE 2 Breast milk compared to formula milk in reducing the severity of NAS.

supported by the clinical experience of the authors.

How the various factors contribute to the alleviation of withdrawal symptoms in NAS is not yet fully understood. Nevertheless, breastfeeding does have positive effects and as a result, it should be strongly promoted.

Challenges to breastfeeding in the substance misusing population

The baseline rates of breastfeeding of substance misusing women are lower than the general population¹¹ and there are a number of challenges to breastfeeding in this group of women. This is multifactorial, reflecting a combination of:

- lack of information
- negative attitudes towards breastfeeding
- an unsupportive social environment
- low motivation to start and continue breastfeeding.

There is a lack of information regarding the additional positive benefits of breastfeeding with regards to NAS in

infants of substance misusing mothers. A review of eight breastfeeding-related leaflets and information provided by national agencies and on reputable websites provides no information on the potential additional benefits of breastfeeding in this group of women²⁹⁻³⁶. There is even an active suggestion to not breastfeed³⁶. The authors could not find any dedicated information source regarding breastfeeding in relation to NAS (outside of medical literature) that would be readily available to the general population.

In Leeds, before commencement of the promotion of breastfeeding for substance misusing mothers, a survey was conducted to ascertain the attitudes of healthcare professionals towards feeding infants at risk of NAS. The thirty medical and nursing staff surveyed revealed negative attitudes towards recommending and promoting breastfeeding in this group of women. Thirteen per cent of those surveyed felt breastfeeding should not be

encouraged in drug-using mothers and 11% believed that breastfeeding is harmful for infants if their mothers are drug users. Only 23% of respondents strongly agreed that breastfeeding should be promoted for these infants. Hence lack of information about the benefits of breastfeeding and lack of supportive attitudes among healthcare professionals are major contributing factors to low breastfeeding rates in substance misusing mothers.

HIV is the only medical contraindication to breastfeeding in substance misusing mothers. Factors such as the use of street drugs or polydrug use can pose additional challenges to the promotion of breastfeeding but do not provide a clear contraindication, however this is not universally agreed and views differ among professionals regarding polydrug use. The American College of Obstetricians and Gynecologists committee recommends that women should be counselled that methadone and buprenorphine are found in breast milk regardless of the maternal

Citation	Study group	Key results
Begg et al ¹⁹	Eight lactating mothers on a methadone maintenance programme and their infants	The estimated doses of R- and S-methadone received by the infant via immature milk were low (relative infant dose was 2.8% of the maternal dose).
Jansson et al ¹⁴	Eight substance misusing mothers paired with breastfeeding women who exclusively formula fed their infants.	Very low levels of methadone excreted in the breast milk and in infant blood samples. No significant difference in neurobehavioral assessments between the two groups.
Blinick et al ²⁰	Ten women using methadone	The methadone levels in breast milk were low (0.05-0.57µg/mL) with an average milk to plasma ratio of 0.83. Increased methadone doses generally resulted in higher breast milk levels but not linearly.
Pond et al ²¹	Two methadone-maintained women	Milk to plasma ratios were constant at 0.32 and 0.61 respectively. The estimated daily intake of methadone by infants was only 0.01-0.03mg.
Kreek et al ²²	Two women on methadone maintenance therapy	Milk to plasma ratios of 0.05-1.2.
Wojnar-Horton et al ²³	Twelve breastfeeding women on methadone therapy and eight of their infants	The mean (95% CI) milk to plasma ratio was 0.44 (0.24-0.64). The calculated exposure of the infants was 17.4µg/kg/day. The mean dose of methadone in breast milk was 2.79% of the maternal dose.
Geraghty et al ²⁴	Two women	The average milk to plasma ratios for the two mothers were very small (0.661 and 1.215 respectively).
McCarthy et al ²⁵	Eight women maintained on methadone	Methadone levels in milk ranged from 27-260ng/mL, with a mean level for the group of 95ng/mL. The calculated mean daily methadone ingestion was 0.05mg/day.

TABLE 3 A summary of studies of methadone concentrations in breast milk.

dose³⁷. They further recommend that breastfeeding should be encouraged in those patients who are not HIV positive, who are not using additional drugs and who have no other contraindications³⁷. In some cases, custody issues and foster care present additional challenges in relation to breastfeeding, and these should be addressed on a case-by-case basis.

How to promote breastfeeding

Both drug-dependent women and the staff caring for them need targeted intervention and education in order to improve breastfeeding rates. There is little benefit in promoting breastfeeding within the antenatal clinic of the addiction unit if the postnatal staff do not have the knowledge and skills to support breastfeeding. For this reason, a staff training programme has been introduced at Leeds incorporating the use of information flyers (**FIGURE 3**) and a short lecture within the mandatory breastfeeding study day. The hope is that staff attitudes towards breastfeeding will improve and contribute to higher breast-feeding rates in substance misusing mothers. This will be assessed in due course.

There is extensive literature available regarding promotion of breastfeeding in the general population³⁸⁻⁴⁰ in which the underlying theme is a heterogeneity of interventions showing a varying degree of effect on breastfeeding rates. The authors were unable to find any literature regarding breastfeeding promotion strategies targeted exclusively towards drug-dependent mothers. It can be assumed that the effects of the various breastfeeding promotion strategies may be different in this challenging population of women and hence there is an argument for more research to assess which breastfeeding promotion strategies are most effective in drug-dependent women.

While breast milk ameliorates the severity of NAS, it is unlikely to completely prevent it. Drug-dependent women are likely to require intensive and specific breastfeeding support. They also need clear advice to not abruptly discontinue breastfeeding in order to avoid the risk of subsequent rebound withdrawal.

Conclusion

There are definite benefits of breastfeeding in mitigating the severity of NAS. The

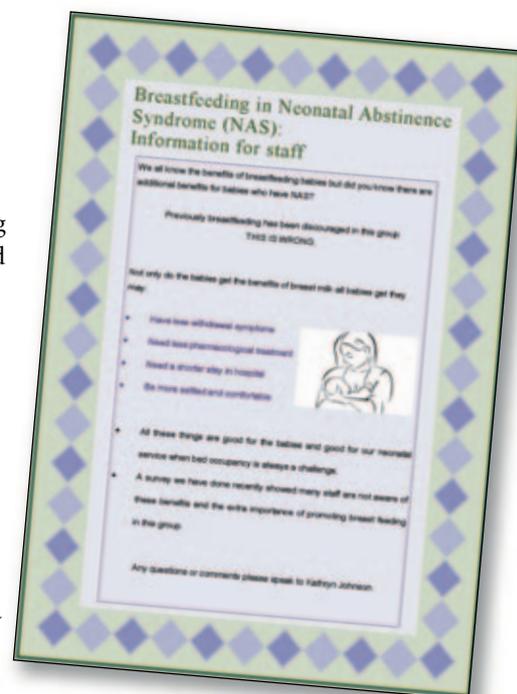


FIGURE 3 The information sheet for nursing staff.

literature strongly suggests positive outcomes including fewer symptoms, reduced need for and duration of pharmacological treatment and shorter hospital stay.

Breastfeeding rates in drug-dependent women are extremely low and there are significant challenges to promotion of breastfeeding in this group, however through staff education and provision of supportive information to drug-dependent women, it may be expected that rates significantly improve thereby helping a vulnerable group of infants.

References

1. **NHS National Treatment Agency For Substance Misuse.** *Statistics from the National Drug Treatment Monitoring System* [Online]. Available from: www.nta.nhs.uk/statistics.aspx [Accessed 9 Dec 2013].
2. **NICE.** Clinical guidance CG110. *Pregnancy and Complex Social Factors: A Model for Service Provision for Pregnant Women with Complex Social Factors* [Online]. 2010. Available from: <http://guidance.nice.org.uk/CG110> [Accessed 2 Dec 2013].
3. **Dryden C., Young D., Hepburn M., Mactier H.** Methadone use in pregnancy: factors associated with the development of neonatal abstinence syndrome and implications for healthcare resources. *BJOG* 2009;116:655-71.
4. **Sherwood R.A., Keating J., Kavvadia V., Greenough A., Peters T.J.** Substance misuse in early pregnancy and relationship to fetal outcome. *Eur J Pediatr* 2009;158:488-92.
5. **Mactier H.** The management of heroin misuse in pregnancy: Time for a rethink? *Arch Dis Child Fetal Neonatal Ed* 2011;96:F457-60.
6. **Coghlan D., Milner M., Clarke T. et al.** Neonatal abstinence syndrome. *Ir Med J* 1999;92:232-33, 236.
7. **Johnson K., Greenough A., Gerada C.** Maternal drug use and length of neonatal unit stay. *Addiction* 2003;98:785-89.
8. **Bio L.L., Siu A., Poon C.Y.** Update on the pharmacologic management of neonatal abstinence syndrome. *J Perinatol* 2011;31:692-701.
9. **Hudak M.L., Tan R.C., Committee on Drugs, Committee on Fetus and Newborn, American Academy of Pediatrics.** Neonatal drug withdrawal. *Pediatrics* 2012;129:e540-60.
10. **Velez M., Jansson L.M.** The opioid dependent mother and newborn dyad: non-pharmacologic care. *J Addict Med* 2008;2:113-20.
11. **Wachman E.M., Byun J., Philipp B.L.** Breastfeeding rates among mothers of infants with neonatal abstinence syndrome. *Breastfeed Med* 2010;5: 159-64.
12. **Schardt C., Adams M.B., Owens T. et al.** Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Med Inform Decis Mak* 2007;7:16. doi:10.1186/1472-6947-7-16.
13. **Abdel-Latif M.E., Pinner J., Clews S. et al.** Effects of breast milk on the severity and outcome of neonatal abstinence syndrome among infants of drug-dependent mothers. *Pediatrics* 2006;117: e1163-69.
14. **Jansson L.M., Choo R., Velez M.L. et al.** Methadone maintenance and breastfeeding in the neonatal period. *Pediatrics* 2008;121:106-14.
15. **Isemann B., Meinzen-Derr J., Akinbi H.** Maternal and neonatal factors impacting response to methadone therapy in infants treated for neonatal abstinence syndrome. *J Perinatol* 2011;31:25-29.
16. **McQueen K.A., Murphy-Oikonen J., Gerlach K., Montelpare W.** The impact of infant feeding method on neonatal abstinence scores of methadone-exposed infants. *Adv Neonatal Care* 2011;11:282-90.
17. **Pritham U.A., Paul J.A., Hayes M.J.** Opioid dependency in pregnancy and length of stay for neonatal abstinence syndrome. *J Obstet Gynecol Neonatal Nurs* 2012;41:180-90.
18. **Welle-Strand G.K., Skurtveit S., Jansson L.M. et al.** Breastfeeding reduces the need for withdrawal treatment in opioid-exposed infants. *Acta Paediatr* 2013;doi: 10.1111/apa.12378.
19. **Begg E.J., Malpas T.J., Hackett L.P., Ilett K.F.** Distribution of R- and S-methadone into human milk during multiple, medium to high oral dosing. *Br J Clin Pharmacol* 2001;52:681-85.
20. **Blinick G., Inturrisi C.E., Jerez E., Wallach R.C.** Methadone assays in pregnant women and progeny. *Am J Obstet Gynecol* 1975;121:617-21.
21. **Pond S.M., Kreek M.G., Tong T.G. et al.** Altered methadone pharmacokinetics in methadone maintained pregnant women. *J Pharmacol Exp Ther* 1985;233:1-6.
22. **Kreek M.J., Schecter A., Gutjahr C.L. et al.** Analyses of methadone and other drugs in maternal and neonatal body fluids: Use in evaluation of symptoms in a neonate of mother maintained on methadone. *Am J Drug Alcohol Abuse* 1974; 1:409-19.
23. **Wojnar-Horton R.E., Kristensen J.H., Yapp P. et al.** Methadone distribution and excretion into breast milk of clients in a methadone maintenance programme. *Br J Clin Pharmacol* 1997;44:543-47.
24. **Geraghty B., Graham E.A., Logan B., Weiss E.L.** Methadone levels in breast milk. *J Hum Lact* 1997; 13:227-30.
25. **McCarthy J.J., Posey B.L.** Methadone levels in human milk. *J Hum Lact* 2000;16:115-20.
26. **Saiki T., Lee S., Hannam S., Greenough A.** Neonatal abstinence syndrome – postnatal ward versus neonatal unit management. *Eur J Pediatr* 2010; 169:95-98.
27. **Oei J., Lui K.** Management of the newborn infant affected by maternal opiates and other drugs of dependency. *J Paediatr Child Health* 2007;43:9-18.
28. **Malpas T.J., Darlow B.A.** Neonatal abstinence syndrome following abrupt cessation of breastfeeding. *N Z Med J* 1999;112:12-13.
29. **NHS.** *Off to the Best Start – Important Information About Feeding your Baby* [Online]. Available from: www.nhs.uk/start4life/Pages/breastfeeding-benefits.aspx [Accessed 9 Dec 2013].
30. **NHS choices.** *Why breastfeed?* [Online]. Available from: www.nhs.uk/conditions/pregnancy-and-baby/pages/why-breastfeed.aspx#close [Accessed 9 Dec 2013].
31. **Association of Breastfeeding Mothers.** *Breastfeeding Information*. [Online]. Available from: <http://abm.me.uk/breastfeeding-information/> [Accessed 9 Dec 2013].
32. **Unicef.** *Baby and You: Your Breastfeeding Journey* [Online]. Available from: http://live.unicef.org.uk/Documents/Baby_Friendly/Leaflets/baby_and_you_breastfeeding_journey.pdf [Accessed 9 Dec 2013].
33. **The National Childbirth Trust.** *Why Breastfeed?* [Online]. Available from: www.nct.org.uk/parenting/why-breastfeed [Accessed 9 Dec 2013].
34. **La Leche League Great Britain.** *Beginning Breastfeeding* [Online]. Available from: www.laleche.org.uk [Accessed 9 Dec 2013].
35. **NHS.** *Breastfeeding* [Online]. Available from: www.breastfeeding.nhs.uk [Accessed 9 Dec 2013].
36. **Patient.** *Breastfeeding* [Online]. Available from: www.patient.co.uk/health/breast-feeding [Accessed 9 Dec 2013].
37. **American College of Obstetricians and Gynecologists.** Opioid abuse, dependence, and addiction in pregnancy. Committee Opinion No. 524. *Obstet Gynecol* 2012;119:1070-76.
38. **Demirtas B.** Strategies to support breastfeeding: a review. *Int Nurs Rev* 2012;59:474-81.
39. **Fairbank L., O'Meara S., Renfrew M.J. et al.** A systematic review to evaluate the effectiveness of interventions to promote the initiation of breastfeeding. *Health Technol Assess* 2000;4:1-171.
40. **Guise J.M., Palda V., Westhoff C. et al.** The effectiveness of primary care-based interventions to promote breastfeeding: systematic evidence review and meta-analysis for the US Preventive Services Task Force. *Ann Fam Med* 2003;1:70-78.

Want to be the first to know what's been published in the latest issue of *Infant*?

Sign up to our *Infant* email update service at www.infantgrapevine.co.uk

The advertisement shows a close-up of a baby's face on the left. On the right, there are three overlapping covers of the magazine 'Infant'. The top cover is titled 'FOCUS ON RUKUNGIRI, UGANDA'. The middle cover features a photo of a baby and the title 'Vitamin D deficiency in infants'. The bottom cover has the title 'infant' in large blue letters and the subtitle 'for neonatal and paediatric healthcare professionals'. Below the covers, there is a small text box: 'Editorial: Concerns with the NICE guideline on seeping and holding a dead baby'.