NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Centre for Clinical Practice

Review consultation document

Review of Clinical Guideline (CG93) – Donor breast milk banks: the operation of donor milk bank services

Background information

Guideline issue date: 2010

2.5 year review: 2012 (first review)

National Collaborating Centre: Internal Clinical Guideline Programme

1. Consideration of the evidence

Literature search

From a systematic literature search, new evidence was identified that related to the following clinical areas within the guideline:

- **Service descriptions (whole guideline)**
- **Recruitment, assessment and selection of donor women**
    - Recruiting donors
    - Serological testing of potential donors.
- **Collection, storage and handling of donor breast milk**
    - Testing and treatment of donor milk, including pasteurisation

Through this stage of the process, a sufficient number of studies (n=33) relevant to the above clinical areas were identified from the literature search to allow an assessment for a proposed review decision and are summarised in table 1 below.

As CG93 is a service delivery guidance all levels of evidence were considered during the literature review. The majority of studies identified were either primary studies or observational in nature. It was not always possible from the abstract to differentiate the exact study type.

No additional clinical area was identified from initial intelligence gathering, qualitative feedback from other NICE departments and the views expressed by the Guideline Development Group that required further focused literature searches.

All references identified through the literature search and initial intelligence gathering can be viewed in Appendix 1.

Table 1. Summary of articles from the literature search

Clinical area 1: Service descriptions		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Related clinical questions from the guideline n/a **Relevant section of guideline and recommendations** **2**	Through an assessment of the abstracts from the literature search 8 service descriptions or position statements were identified from the following countries: UK[1], Norway[2], US[3,4], Canada[5] and not stated in 3 studies[6,7,8]. • A descriptive study which assessed feasibility of providing donor breast milk to infants in a resource limited Neonatal Premature Unit (NPU)[1]. • A narrative article on the donor milk banks in Norway[2]. • An article that described the steps taken and the obstacles overcome to initiate a human milk bank in an neonatal intensive care unit in the US[3]. • An article that provided guidelines and practical suggestions for establishing a donor human milk depot in North America[4].	No new evidence was identified which would invalidate current guideline recommendations.

	• A narrative summary of human milk banking in Canada[5]. • A descriptive study which characterized the behaviour of human milk donation and described the informal social and formal institutional support for donors[6]. • An article which discussed the implementation of a donor program for pasteurised donor breast milk in the NICUs of 3 hospitals[7]. • An observational study describing an approach undertaken by one service to reduce the volume donated human milk discarded by a service due to been unsuitable for consumption[8]. **Summary** A number of service descriptions highlighting challenges, practices and population based issues from a variety of cultural and national perspectives were identified. The abstracts did not provide any evidence that would invalidate the current guideline CG 93. However, in the current process as only an assesssment of abstracts is undertaken it is not possible to determine if the service descriptions identified fully support or provide contradictory evidence to the service described in CG93.	

Clinical area 2: Recruiting donors		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Related clinical questions from the guideline How should donor women be recruited, and what information should be provided? The needs of different ethnic, religious and cultural groups will be considered **Relevant section**	Through an assessment of the abstracts from the literature search 4 studies relevant to the clinical question were identified. Three opinion pieces and 1 service description were identified that had addressed the cultural and religious implications of donor breast milk for individuals of the Muslim faith [9],[10,11,12]. The 3 opinion pieces discussed the issues concerning and potential ways to overcome the religious reservations due to 'milk kinship' and subsequent implications for marriage in Islamic Law that human milk banks face. The fourth article described a human milk donation system established in an Malaysian hospital as an option to address the problems associated with milk kinship for hospitals without a human milk bank or in the Muslim community[12]. **Summary** Evidence relating to 'kinship' in Islamic Law was noted in the evidence base for the orginal guideline. The GDG suggested that milk banks should use a flexible approach	No new evidence was identified which would invalidate current guideline recommendations.

of guideline and recommendations 2.5	for recruitmentof donors	
Clinical area 3: Screening and selecting donors		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Related clinical questions from the guideline What factors should be assessed to determine the suitability of potential donors? What initial and repeat serological testing should be undertaken:	Through an assessment of the abstracts from the literature search 2 studies relevant to the clinical question were identified. A 6 year retrospective review of donor serological testing at a human milk bank in the US reported a significant incidence of positive serology among women interested in donating human milk. This included samples positive for syphilis, hepatitis B, hepatitis C, HTLV and HIV[13]. One primary study evaluated the frequency of detection of HBV surface antigen and HBV-DNA in colostrum of HBV-infected nursing mothers before and after Holder pasteurization. Before and after pasteurization at least one marker was detected in 83% milk samples. As HBV is highly contagious these findings show the importance of	No new evidence was identified which would invalidate current guideline recommendations.

Relevant section of guideline recommendations **2.6**	serological screening of human milk bank donors[14]. **Summary** The guideline recommends a stepped screening process which includes serological testing for all the infectious diseases mentioned in the two identified articles.	
Clinical area 4: Milk handling in general		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Related clinical questions from the guideline What are the best (safest) methods for collecting, storing and handling donor breast milk?	Through an assessment of the abstracts from the literature search 6 studies relevant to the clinical question were identified. **Six primary studies were identified that related to storage of collected donor breast milk samples:** • One study which evaluated the effect of cold storage on the natural bacterial composition of breast milk indicated that cold storage of milk at -20 °C for 6	No new evidence was identified which would invalidate current guideline recommendations.

Relevant section of guideline recommendations **2.10, 2.11, 2.12, 2.13, 2.14,**	weeks does not significantly affect either the quantitative or the qualitative bacterial composition of breast milk[15]. • A further primary study investigated refrigerator storage of human milk at 4 °C for bacterial growth, cell counts, and component concentrations during 96 hours. The authors concluded that in this timeframe changes were minimal and the overall integrity of milk during refrigerator storage was preserved[16]. • One primary study indicated that the storage of human breast milk at -80°C over 2 months results in decreased antioxidant capacity however the antioxidant capacity of human colostrum did not change by storage at -80°C [17]. A second study indicated that freezing induces losses in the antioxidant properties of breast milk. However, these were minimised by storage at -80°C for shorter periods of time compared to storage at -20°C [18]. • One study assessed the impact of pasteurization or prolonged storage at -20°C on the immunologic components of human milk and the capability of the different forms of human milk to support bacterial proliferation. The immunomodulatory proteins in human milk were reduced by pasteurization and, to a lesser extent, by frozen storage for 4 weeks at -20°C with both resulting in decreased antibacterial capability[19]. One primary study found that human colostrum can be	

	stored at 4°C for up to 48 h or at -20 °C or -80°C for at least 6 months without losing its immunological properties[20]. **Summary** The Guideline makes numerous recommendations relating to cold storage of donor milk samples based on the location of the sample (domestic or bank) and the access for the donor to refrigeration equipment. However, the main recommendation is to advise donors to freeze and transport expressed milk samples as soon as possible to the milk bank. In this setting frozen milk can be stored for up to 3 months. Donor samples at the milk bank should be stored at -20°C for up to 3 months prior to pasteurisation. The evidence identified as part of the review highlights many of the factors which were recognised during the development of the guideline. However, overall the GDG considered the safety of the milk (level of bacterial contamination) to be paramount. They noted that storage methods may damage nutritional and immunological components of the donor milk but made pragmatic recommendations for refrigeration and freezing. In light of this the new evidence does not contradict current recommendations.	
Clinical area 5: Testing and treating		

Clinical question	Summary of evidence	Relevance to guideline recommendations
Related clinical questions from the guideline How should donor milk be tested and treated? **Relevant section of guideline recommendations** **2.16, 2.17**	Through an assessment of the abstracts from the literature search 13 studies relevant to the clinical question were identified **Testing (2 studies)** One study investigated the pathogenic potential of the Bacillus population that may survive Holder pasteurisation of human milk and to evaluate the nutritional damage of this treatment using the furosine and lactulose indexes. Holder pasteurisation led to the destruction of bacteria present initially in donor milk samples, except for some *B. cereus* in the minority of samples. Pasteurisation did not significantly alter the concentration furosine or lactulose[21]. The audit results from a donor milk bank for bacterial contamination both before and after Holder pasteurization over a 3 year period were reported in an article. Before pasteurization a wide variety of bacteria were found to contaminate human milk from donor mothers. After routine Holder pasteurization of donor milk, 93% of milk samples	No new evidence was identified which would invalidate current guideline recommendations.

	showed no growth on routine bacterial cultures[22]. **Treating (11 primary studies)** ***Nutritional and immunological components of donor milk (pasteurisation)*** • One study reported that the immunomodulatory proteins in human milk were reduced by pasteurization and, to a lesser extent, by frozen storage at -20°C, resulting in decreased antibacterial capability[19]. • One study showed that Holder pasteurization significantly reduced the concentration of several immunoactive compounds but did not affect granulocyte colony-stimulating factor, heparin-binding epidermal-like growth factor and hepatocyte growth factor present in breast milk[23]. • An investigation found that Holder pasteurisation reduced milk adiponectin and insulin in donor human milk[24]. • Holder pasteurization significantly reduced the concentrations of erythropoietin and Interleukin-10, whereas lesser degrees of heating increased the detection of Interleukin-10 in the aqueous phase of donor term human breast milk [25].	

	• The fatty acid and amino acid compositions in donor milk samples were not affected by pasteurization but had low concentrations of docosahexaenoic acid and amino acids[26]. • A study which determined the effect of various processes (Holder pasteurization, freezing and thawing and feeding method) on the macronutrient concentration of human milk. Determined that there was significant reduction of fat and protein following pasteurization. Thawing speed did not affect the macronutrients concentrations[27]. ***Pasteurisation processes*** The following primary studies compared various methods for pasteurisation/ treatment of donor human breast milk: • One study on Holder pasteurization compared different temperatures to ascertain the optimum conditions for retaining immunological and nutritional components. Pasteurisation at 57°C for 30 min was also effective at removing the inoculated bacterial species and had a significantly higher proportion of	

	lysozyme compared to other methods[28]. • A study found that high-temperature short-time pasteurization preserved the integrity of bile salt-stimulated lipase in comparison to Holder pasteurization in human donor milk [29]. • A study which compared artificially contaminated human milk samples treated with ultrasound with and without and heating (thermoultrasound) was identified. The study indicated that thermoultrasonic treatment was a more effective method for pasteurizing donor human milk and retaining a greater proportion of bioactive components compared with current practices[30]. • One study found that high-pressure processing maintained vitamin C and ascorbic acid levels better than Holder pasteurisation. However the fatty acid proportions delta-, gamma-, and alpha-tocopherols in milk did not vary with either treatment[31]. • Comparison of high-pressure/low temperature processing to heat treatment at 62.5C on milk. The results indicated that a pressure treatment at 00Pa for 5min and 12C maintained the immunological protective capacity (IgA) in the milk	

	samples better than heat treatment[32]. • One study evaluated a method for reducing the variation in fat and energy content of human milk prior to fortification by centrifugation to produce a layer of cream which was then resuspended to produce reconstituted milk of a specified standard fat content. Using this method it was possible to reduce the coefficient of variation in fat content of donor human milk samples[33]. **Summary** A number of new techniques were identified to pasteurise donor breast milk. From an assessment of the abstracts it was not possible to assess in all cases if these were effective at removing the microbial contamination although the effects on various other milk components were often mentioned. The evidence within the guideline detailed numerous methods of pasteurisation including high pressure methods and various temperatures and detailed the consequences on immunological and nutritional components. The GDG noted that the pasteurisation method needed to balance safety with the destruction or reduction in the nutritional and immunological components of donor milk. CG93 recommends	

	pasteurising donated milk at 62.5°C for 30 minutes.	

No recent or ongoing clinical trials were identified that were within the scope of the guideline.

New evidence was identified that was relevant to 1 research recommendation in the original guideline:

- The process of handling donor milk: What is the effect of the process of milk banking on the nutritional and immunological components of donor milk? The new evidence detailed the consequences on immunological and nutritional components however often failed to detail microbial consequences of the treatment in the abstracts (summarised in table 1). The GDG noted that the pasteurisation method needed to balance safety with the destruction or reduction in the nutritional and immunological components of donor milk.

In conclusion, no identified new evidence contradicts current guideline recommendations.

Guideline Development Group, Service provider and National Collaborating Centre perspective

A questionnaire was distributed to GDG members, the National Collaborating Centre and the milk bank service providers to consult them on the need for an update of the guideline. Nine responses were received with all respondents highlighting that there was no new evidence related to the guideline that supports or contradicts current guideline recommendations or any interventions that have became more cost-effective or are likely to become more cost-effective.

Only 2 ongoing trials were highlighted: a study on the effect of different types of pasteurisation and its effect on the components of human milk and a study investigating the nutritional content of donor breast milk. Additionally three publications on areas outside the scope of the current guideline were

submitted. These included a study on sterility of donor breast milk post thawing and use in a neonatal unit was provided and two publications relating to the overall ethical issues associated with donor milk[34,35,36].

No variations or substantial changes to management, costs or organisation of care recommended by the current guidelines were reported. Nor were there any reports of any new national policies or audits or efficacy or safety concerns about the recommended practice. However a number of practice issues were highlighted:

- Exclusion criteria for donors
    - whom have received in *vitro fertilisation* and the medicines, donor eggs, donor sperm.
    - Variant Creutzfeldt Jakob disease risk stratification via the Health Protection Agency website.
- Defrosting conditions for donor milk.
- Cooling temperatures for pasteurised donor milk

The respondents felt the exclusions listed in the scope of the original guideline were still justified. With regard to current inequalities in access to services or service provision not addressed in the current guideline 2 respondents suggested that as the guideline does not address which infants should receive donor breast milk and its availability which could potentially result in inequities in access to this resource. However, indications for use of donor breast milk were outside of the scope of the guideline.

Overall, 4 respondents felt that the guideline did not require an update at this time. Conversely, 4 suggested partial updates looking at the practice issues mentioned around IVF, medication and Creutzfeldt Jakob disease risk stratification. One respondent indicated that they wished the guideline to be updated to include staff training, however which specific aspects of training

were not specified. Milk bank staff training is an area currently covered in section 2.2 of the guideline.

Implementation and post publication feedback

In total 19 enquiries were received from post-publication feedback, of which were routine.

The NICE implementation programme has not identified any routinely collected data to determine the uptake of this clinical guideline:

Qualitative input from the implementation field team recorded the following feedback in relation to this guidance: The guideline was well received and has elevated the profile and importance of milk banks within the NHS. This has enabled management buy-in and ensured appropriate staff training and funding of such a “special” service. However, others stakeholders have commented that if unsupported or underfunded then milk banks struggle to implement the guideline due to lack of resources, low service profile and lack of competent staff.

Relationship to other NICE guidance

The following NICE guidance is related to CG93:

Guidance	**Review date**
PH11Maternal and child nutrition. NICE public health guidance 11 (2008)	July 2014
CG37 Postnatal care (2006)	July 2015.

There are 2 topics on the NICE quality standards topic library that have been referred that may have overlap with CG93:

Premature birth. Quality Standard

Parenteral nutrition in neonates. Quality Standard

Anti-discrimination and equalities considerations

No evidence was identified to indicate that the guideline scope does not comply with anti-discrimination and equalities legislation.

Conclusion

The evidence and intelligence identified through the update review process indicate that there are no additional areas which would indicate a significant change in clinical practice. There are no factors described above which would invalidate or change the direction of current guideline recommendations.

Review recommendation

The guideline should not be considered for an update at this time.

Centre for Clinical Practice
22nd October 2012

Appendix I

1 . Coutsoudis I, Adhikari M, Nair N et al. (2011) Feasibility and safety of setting up a donor breastmilk bank in a neonatal prem unit in a resource limited setting: An observational, longitudinal cohort study. BMC Public Health 11:356-

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3 . Kamholz KL, Parker MG, and Philipp BL. (2012) Implementing change: steps to initiate a human donor milk program in a US Level III NICU. Journal of Human Lactation 28:128-131.

4 . Geraghty SR, List BA, and Morrow GB. (2010) Guidelines for establishing a donor human milk depot. Journal of Human Lactation 26:49-52.

5 . Kim J and Unger S. (2010) Human milk banking. Paediatrics & Child Health 15:595-602.

6 . De Alencar LC and Seidl EM. (2010) Breast milk donation and social support: reports of women donors. Revista Latino-Americana de Enfermagem 18:381-389.

7 . Rosenbaum K. (2012) Implementing the use of donor milk in the hospital setting: implications for nurses. Nursing for Women's Health 16:202-208.

8 . Grazziotin AL, Grazziotin MC, and Letti LA. (2010) Disposal of human milk donated to a human milk bank before and after measures to reduce the amount of milk unsuitable for consumption. Jornal de Pediatria 86:290-294.

9 . El-Khuffash A and Unger S. (2012) The concept of milk kinship in islam: issues raised when offering preterm infants of muslim families donor human milk. Journal of Human Lactation 28:125-127.

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16 . Slutzah M, Codipilly CN, Potak D et al. (2010) Refrigerator storage of expressed human milk in the neonatal intensive care unit. Journal of Pediatrics 156:26-28.

17 . Sari FN, Akdag A, Dizdar EA et al. (2012) Antioxidant capacity of fresh and stored breast milk: is -80degreesC optimal temperature for freeze storage? Journal of Maternal-Fetal & Neonatal Medicine 25:777-782.

18 . Silvestre D, Miranda M, Muriach M et al. (2010) Frozen breast milk at -20 degrees C and -80 degrees C: a longitudinal study of glutathione peroxidase activity and malondialdehyde concentration. Journal of Human Lactation 26:35-41.

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28 . Czank C, Prime DK, Hartmann B et al. (2009) Retention of the immunological proteins of pasteurized human milk in relation to pasteurizer design and practice. Pediatric Research 66:374-379.

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