Dissertation

Heat treatment of expressed breast milk as in-home procedure to limit mother-to-child transmission of HIV: A systematic review

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Abbreviations

ADA	American Dietetic Association
AIDS	Acquired immune deficiency syndrome
CASP	Critical Appraisal Skills Programme
EBM	Expressed breast milk
EBP	Evidence-based practice
EBF	Exclusive breast feeding
FH	Flash-heating
HCPRDU	Health Care Practice Research and Development Unit
HIV	Human immunodeficiency virus
HTEBM	Heat-treated expressed breast milk
IgA	Immunoglobulin A
IgG	Immunoglobulin G
JBIEBNM	The Johanna Briggs Institute for Evidence Based Nursing and Midwifery
MTCT	Mother-to-child transmission
NDoH	National Department of Health
OED	Oxford English Dictionary
PMTCT	Prevention of mother-to-child transmission
PHRU	Public Health Resource Unit
PP	Pretoria pasteurization
WHO	World Health Organization

Abstract

Mother-to-child transmission (MTCT) of HIV is the *most significant source of HIV infection* in young children. As the HI virus has been identified in cell-free and cell-associated compartments of breast milk, it is clear that breast milk is one of the ways in which mother-to-child transmission of HIV can take place in addition to in utero and intrapartum transmission.

While breastfeeding carries the risk of HIV transmission, *not breastfeeding* carries significant health risks for infants and young children, such as an increased risk of diarrhoea and pneumonia, morbidity and mortality.

When an HIV-positive mother decides to breastfeed her baby, pasteurisation of expressed breast milk (EBM) could be a possible infant-feeding option to limit transmission of the HI virus through breast milk, since this method has shown to effectively inactivate HIV type 1. Three methods of pasteurisation of human milk were investigated in this study: *Holder pasteurisation*, *flash-heating* and *Pretoria pasteurisation*.

The systematic review is a helpful method to summarise the best-quality empirical evidence of the benefits and limitations of a specific method, such as heat treatment, and to provide recommendations for future research. Therefore, the aim of this study was to critically synthesise by means of a systematic review the best available existing evidence and to provide a clear overview of the effectiveness of heat treatment of EBM as an in-home procedure to inactivate the HI virus, and in so doing limit mother-to-child transmission of HIV. This study provides the clinical practitioner with accessible information on the effectiveness of heat treatment of EBM as an in-home procedure in terms of (1) safety, inactivation of the HI virus and retaining the protective and nutritional value of the EBM; (2) feasibility as an in-home procedure; and (3) acceptability by the mothers and their communities. This information could be used to improve clinical practitioners' knowledge and include it in their health education to contribute to the prevention of mother-to-child transmission.

This study is based on the framework of the model for evidence-based clinical decisions of Haynes, Devereaux and Guyatt (2002).

The search strategy was conducted in March/April 2009. The initial search resulted in 574 articles. After thorough screening of potentially relevant studies on heat treatment of EBM, the studies that met the inclusion criteria were critically appraised and scored based on their methodological qualities using standardised instruments. After 6 months, the search was updated. The search obtained 1 article. The final sample involved 12 articles.

Conclusions were integrated and synthesised as a basis for developing a clear overview of the best available existing evidence. Finally, the findings of the study were synthesised and the research was evaluated, a conclusion was given, limitations were identified and recommendations were formulated for nursing practice, education and research.

The bottom-line answer concluded that heat treatment of EBM should be emphasised as a safe alternative for feeding exposed infants (those of an HIV-positive mother, those of uncertain HIV status or during weaning if the mother cannot afford formula or cow's milk), but should be supported with appropriate information to the individual mother, her family and the community. Overall it can be concluded that existing evidence of the effectiveness (in terms of *safety, feasibility* and *acceptability*) of heat treatment of EBM, particularly Pretoria pasteurisation, used as a simple in-home procedure, is insufficient, and further research is required.

Keywords: heat treatment, expressed breast milk, in-home procedure, HIV-positive mothers, mother-to-child transmission, systematic review

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CHAPTER 1:

OVERVIEW

1.1 INTRODUCTION

The aim of this study was to critically appraise and synthesise by means of a systematic review the best available existing evidence of the effectiveness of heat treatment of expressed breast milk (EBM) as a simple in-home procedure to inactivate the HI virus. The systematic review is a helpful method to summarise the best-quality empirical evidence of the benefits and limitations of a specific method, such as heat treatment (Kitchenham, 2004:3) and to provide recommendations for future research. It can furthermore educate clinical practitioners and keep them up to date, and also aims to translate research evidence to assist in evidence-based clinical decision making in order to optimise health outcomes (Cook, Greengold, Ellrodt & Weingarten, 1997:210).

During a preliminary review of the literature, the researcher concluded that no systematic review could be found concerning heat treatment of EBM that can be used as an in-home procedure for mothers. Therefore, a systematic review was needed to provide a clear summary of available existing evidence of heat treatment.

This study was positioned within the theoretical framework of the model for evidence-based clinical decisions of Haynes, Devereaux and Guyatt (2002:384) because of the model's suitability to the systematic review method. The model is an integration of four aspects that should be taken into consideration during decision making on best practice: (1) research evidence; (2) clinical state and circumstances; (3) patients' preferences, values and actions; and (4) clinical expertise.

This study provides an overview of the best available evidence of the effectiveness of heat treatment as an in-home procedure. This evidence, expressed in the outcomes of this systematic review, will be submitted for publication in a peer-reviewed journal and therefore made accessible to clinical practitioners to improve their knowledge (which could be included in their health education). It will finally contribute to the prevention of mother-to-child transmission by introducing effective procedures to inactivate the HI virus, such as pasteurisation.

1.2 BACKGROUND

Mother-to-child transmission (MTCT) is the most significant way of transmission of HIV infection in young children (WHO, UNAIDS, UNICEF &UNPF, 2008:1). As the HI virus is found in cell-free and cell-associated compartments of breast milk (Ruf, Coberly, Halsey, Boulos, Desormeaux, Burnley, Joseph, McBrien, Quinn, Losikoff, O'Brien, Louis & Farzadegan, 1994:68; Thiry, Sprecher-Golberger, Jonckheer, Levy, Van de Perre, Henrivaux, Cogniaux-Leclerc & Clumeck, 1985:891), it became clear that breast milk is one of the ways in which mother-to-child transmission of HIV can take place in addition to in utero and intrapartum transmission (Coutsoudis, Goga, Rollins & Coovadia, 2002:154). Breastfeeding, usually the preferred choice of feeding for the newborn infant (WHO *et al.*, 2008:451), therefore might not be the best feeding choice for the infant of an HIV-positive mother.

Factors that increase the risk of HIV transmission through breast milk are, among others, ribonucleic acid (RNA), viral load in plasma and breast milk, health of the mother's breast tissue, duration of breastfeeding and the pattern of infant feeding – exclusive versus mixed feeding (WHO *et al.*, 2008:13).

While breastfeeding carries the risk of HIV transmission, *not breastfeeding* carries other significant health risks to infants and young children, such as an increased risk of diarrhoea and pneumonia, morbidity and mortality (Nicoll, Newell, Peckham, Luo & Savage, 2000:S57; Thior, Lockman, Smeaton, Shapiro, Wester, Heymann, Gilbert, Stevens, Peter, Kim, Van Widenfelt, Moffat, Ndase, Arimi, Kebaabetswe, Mazonde, Makhema, McIntosh, Novitsky, Lee, Marlink, Lagakos & Essex, 2006:794). Most recently, the World Health Organization (WHO) recommended that HIV-infected women should breastfeed their infants exclusively for the first six months of life, unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for them and their infants (WHO *et al.*, 2008:33–36, 43). Only when those conditions can be met, the WHO recommends that HIV-infected women not breastfeed their babies (WHO & UNICEF, 2008:1). However, for infants that have already been diagnosed with HIV, the National Department of Health (NDoH) recommends continuing breastfeeding for at least two years, regardless of whether the mother meets the criteria or not (NDoH, 2008:50).

However, both the WHO and NDoH documents do state that *heat treatment* of human milk could be useful after a period of exclusive breastfeeding in children older than six months to minimise breast milk viral load or as an alternative to breastfeeding during periods of

increased risk, such as when the mother is suffering from mastitis and cracked or bleeding nipples (NDoH, 2008:53; WHO *et al.*, 2008:33–36).

Heat treatment of EBM

Two methods of heat treatment of human milk have been investigated, namely *direct boiling*, which causes significant nutritional damage (Welsh & May, 1979), and *pasteurisation*, which inactivates HIV type 1 (McDougal, Martin, Cort, Mozen, Hedebrant & Evatt, 1985:876), without destroying the essential nutritional elements of breast milk such as vitamins, immunoglobulin A (IgAs), secretory immunoglobulin antibody (SIgA), lactoferrin and lysozyme surviving digestion (Goldblum, Dill, Albrecht, Alford, Garza & Goldman, 1984:380; Israel-Ballard, Abrams, Coutsoudis, Sibeko, Cheryk & Chantry, 2008:444; Israel-Ballard, Chantry, Dewey, Lonnerdal, Sheppard, Donovan, Carlson, Sage & Abrams, 2005:175; Van Zoeren, Schrijver, Van den Berg & Berger, 1987:161).

The following three methods of pasteurisation of human milk have been investigated:

- *Holder pasteurisation* (which is widely used in milk banks), whereby EBM is placed in water that is heated up to 62.5 °C for 30 minutes. This method inactivates HIV type 1 while retaining most of the breast milk's protective elements (Eglin & Wilkinson, 1987:1093; Lawrence & Lawrence, 2005:181; McDougal *et al.*, 1985:876).
- *Flash-heating*, whereby manually expressed human milk in a glass jar is placed (uncovered) in a water bath. When the water begins to boil, the milk is removed from the water bath and heat source immediately and covered with a lid. Once cooled down (to 37 ºC), the human milk is fed to the infant with a cup or spoon (Abrams, 2007:235).
- *Pretoria pasteurisation,* whereby water is boiled in a Hart® 1-litre aluminium pan, after which it is removed from the heat source and a covered jar with human milk (50 ml) is immediately placed in the water for 20 minutes. The jar is then removed from the water bath, where it will be left uncovered to cool down to 37º C (Israel-Ballard *et al*., 2005:176).

Although the Holder pasteurisation method is widely used in milk banks, it is difficult to apply as an in-home method due to the requirements such as gauges and timing devices (Israel-Ballard, Donovan, Chantry, Coutsoudis, Sheppard, Sibeko & Abrams, 2007:318). However, both the flash-heating and Pretoria pasteurisation methods can be used as simple home procedures due to the limited requirements of a glass jar with a fitting lid, a Hart® 1-litre aluminium pan, a stove/fire/hot plate and a cup or spoon (Israel-Ballard *et al*., 2007:318).

The Holder pasteurisation and flash-heating methods have been reported to inactivate HIV while retaining most of the breast milk's protective elements (Eglin & Wilkinson, 1987:1093; Israel-Ballard *et al.,* 2005:178; Lawrence & Lawrence, 2005:181; McDougal *et al.*, 1985:876). Concerning the safety of the Pretoria pasteurisation method, Jeffery, Webber, Mokhondo and Erasmus (2001:348) showed that this method inactivates HIV. Furthermore, Jeffery, Soma-Pillay and Moolman (2003:240) proved in another study, performed in the postnatal ward at a secondary hospital in Pretoria, South Africa, that Pretoria pasteurisation eliminated clinically significant bacteria in 93% of the EBM samples tested. However, according to Israel-Ballard *et al*. (2007:322), further research is needed on the *safety* of heat treatment in general.

Despite the effectiveness of these methods to destroy the HI virus, little is known of the acceptability of pasteurisation as an in-home method. A qualitative study performed by Israel-Ballard, Mathernowskam, Abrams, Morrison, Citibura, Chipato, Chirenje, Padian and Chantry (2006:57) conducted in different areas (rural versus suburban versus urban) in Zimbabwe on the acceptability of heat-treating breast milk (Holder pasteurisation and flash-heating) showed that participants' perceptions of pasteurisation as an in-home treatment changed as a result of increased health education. Participants' enthusiasm for heat treatment increased during the study but was correlated with provided health education.

Other small studies suggest that interest in pasteurisation as an in-home treatment varies depending on region, culture, maternal education and social environment and that barriers to acceptability, such as stigmatisation, cultural beliefs, lack of knowledge and confidence concerning the concept of pasteurisation, should be addressed (Coutsoudis, 2005:958; Leshabari, Koniz-Booher, Astrom, De Paoli & Moland, 2006:10–14). According to Israel-Ballard *et al.* (2006:59), more research on attitudes, barriers and feasibility in different settings is required.

1.3 PROBLEM STATEMENT

Breastfeeding is usually recommended but not safe with regard to MTCT. Heat treatment can offer a safe alternative. Several studies have been done on heat treatment as possible in-home procedure for HIV-positive mothers. However, no systematic reviews in which studies were systematically selected, appraised and summarised were found, thereby indicating a need for such a study. The intention of this study was therefore to establish a critical synthesis of the current evidence base to fill the gap in the literature.

1.4 RESEARCH QUESTION

Against the background and problem statement, the research question was formulated as follows:

How effective is heat treatment of EBM as an in-home procedure in terms of (1) eliminating/ inactivating the HI virus and safety in terms of retaining the protective and nutritional value of the EBM; (2) feasibility as an in-home procedure; and (3) acceptability by the mothers and their communities?

1.5 PARADIGMATIC PERSPECTIVE

The basis for research is a philosophical belief concerning the world, a "worldview" or "paradigm" (LoBiondo-Wood & Haber, 2002:127). The concept 'paradigm' is explained as "a way of viewing a phenomenon or group of phenomena that attracts a group of adherents and raises many questions to be answered" (George, 1990:388). While conducting the research, the researcher develops and reveals certain assumptions. These assumptions are implanted in a philosophical basis, framework or study design (Burns & Grove, 2005:39).

This section explains the paradigmatic perspective of myself as researcher and sets out the central theoretical argument, meta-theoretical assumption and the epistemological assumptions. It also explains the theoretical framework and the methodological assumption of the researcher.

1.5.1 Central theoretical argument

This systematic review provides a summary of the best available evidence of the effectiveness of heat treatment of EBM as an in-home procedure, which, if made assessable to health workers, provides them with assessable information which could be applied in their context.

1.5.2 Meta-theoretical assumption

Meta-theoretical assumptions contain non-epistemic statements that cannot be tested (Mouton & Marais, 1994:192). In nursing research it reflects the researcher's worldview and assumptions of the concepts of man, society, health and nursing. Although these concepts are explained separately below, they are interrelated and collaboratively reflect the researcher's meta-theoretical beliefs.

View of man (human being / individual)

As a nursing researcher I view man as a unique creation with his own rights and responsibilities. The human being is a holistic being with *physiological*, *psychological*, *psychosocial* and *spiritual* dimensions, intrinsically interrelated and dependent.

The *physiological* dimension of a human being relates to possible physiological effects and the influence the disease HIV has as on the health of an HIV-positive mother. It also concerns the possible risk of HIV transmission from mother to child through breastfeeding.

The *psychosocial* dimension refers to the possible concern the mother may have regarding her own health and that of her baby. The HIV-positive mother might be concerned about her and her baby's future. She might be questioning who will take care of the baby when she is not able to due to her health condition.

The *spiritual* dimension links to the possible support or inner strength an HIV-positive mother could experience based on her belief system. Her religion/belief might have a positive influence on helping her to decide how to prevent her child from contracting HIV and to care for her baby in the best possible way. It could also help the HIV-positive mother to think positively of her and her baby's future, despite her health.

Finally, I believe that the HIV-positive mother will choose a feeding option that does not carry the risk of transmitting the HI virus. Therefore, it is important to provide this mother with evidence-based health education to give her the opportunity to make an informed decision regarding safe infant feeding.

View of society

The human being socially interacts and lives in a specific society/environment and therefore will be influenced by the environment and vice versa. This environment might have either a positive or a negative influence on how the human being can maintain a healthy, pleasant and safe life. For the HIV-positive mother, this means that her environment (family, partner, community, etc.) could support or reject her in her decision (of how) to prevent her child from contracting HIV through breast milk. Fear for stigmatisation may prevent the mother from adopting this feeding option, especially in an environment in which breastfeeding is the norm.

View of health

I agree with the definition of the WHO (2001:8) of health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity". However, I think health involves not only psychical, mental and social well-being but also *spiritual* well-being.

Further, I agree with Gupta (2005) that, in order to live a healthy life, basic needs such as water, clothes and food must be met. This means that the HIV-positive mother in particular should meet these basic needs in order to maintain her own health and at the same time care for her infant.

Finally, to maintain a healthy life, I believe that prevention of illness (such as HIV infection) is a major concept within health. Prevention involves the following three dimensions:

- Primary prevention, which concerns the basic prevention of sickness before it develops.
- Secondary prevention, which is synonym for 'screening' and links to measurements that can be performed in order to trace an illness before symptoms occur.
- Tertiary prevention, which is applied in cases when illness occurs to reduce obstructions and thereby increase recovering (Levy, 2009:367–368).

Prevention in the context of the HIV and AIDS pandemic refers to the prevention of MTCT. In the context of MTCT of HIV in a developing country, where replacement feeding is seldom an option, I believe that primary prevention is the most important dimension to prevent HIV and AIDS in the first months of a child's life. By using pasteurisation of EBM as a simple in-home method, the HIV-positive mother can prevent her infant from contracting HIV through breastfeeding.

View of nursing

Nursing entails "the use of clinical judgment in the provision of care to enable people to improve, maintain or recover health to cope with health problems and to achieve the best possible quality of life whatever their disease or disability, until death" (RCN, 2003:527). It uses assessment in the form of clinical judgement and provides care in order for people to improve, maintain or recover health and, linked to that, quality of life. Usually, nursing care is involved in cases when health and therefore quality of life are threatened by "disease" or

"disability" caused by an intra-personal or extra-personal problem (e.g. negative influence from the person's environment).

Providing health education is one way of care in which the nurse can play an important role to improve, maintain or recover health. Health education is defined as follows:

> A process with intellectual, physiological, and social dimensions relating to activities which increase the abilities of people to make informed decisions affecting their personal, family and community well-being. This process based on scientific principles facilitates learning and behavioural change in both health personnel and consumers, including children and youth (Joint Committee on Health Education Terminology, 1973:63).

I believe that health education, when provided to the HIV-positive mother and infant in her social environment, increases her ability to make an informed decision regarding safe, feasible and acceptable infant feeding that positively affects the well-being of her baby. Health education should be based on the best available scientific evidence gleaned from good research (see *epistemological assumptions*).

In order to deliver evidence-based care (e.g. in the form of health education), nurses should be involved in nursing research by, among other things, keeping up to date with the scientific literature and developing critical analytical thinking skills.

Epistemological assumptions

As a nursing researcher, I find it important to conduct research in such a way that findings/outcomes of research can be implemented into practice. Therefore the best evidence-based care must be provided to improve health outcomes. For this study it means that I conducted this research as honestly and rigorously as possible so that the summary of best-quality evidence in this study can be published. By submitting the outcomes of this study for publication in a peer-reviewed journal, this evidence will be made assessable to health workers to include in their health education provided to HIV-positive mothers to limit MTCT of HIV. I believe that 'best' research is research that best answers the appropriate and relevant research question. For the research question in this study (see paragraph 1.4), both quantitative (preferably randomised controlled trials [RCTs] concerning clinical effectiveness) and qualitative studies (views of mothers concerning feasibility and acceptability) were necessary (see paragraphs 1.7 and 2.3.3, and Table 4.1). However, the problem exists that in the hierarchy of types of studies (on which levels of evidence is based), systematic reviews and RCTs (or RCTs based on systematic review) as research

methods are always considered best to answer the research question. This is in contradiction to the statement that what is 'best' should depend on the question stated. For example, when an RCT is not the best method to answer the research question stated, another method, such as a case study, which is considered as 'lower' in the hierarchy of evidence but provides a better method to answer the question, is recommended. Furthermore, the qualities of the researcher (which involves among other things being scientifically honest, ethical and critical) are important to conduct good research. The ethical qualities of the researcher in conducting this study are explained later (see paragraph 1.9) and were ensured due to supervision by researchers with experience in conducting systematic reviews.

1.5.3 Theoretical framework

This study is positioned in the model for evidence-based clinical decisions developed by Haynes *et al.* (2002:385). Evidence-based practice (EBP) is a concept that is often linked to systematic reviews. The aspects of the model of EBP are explained below, including how they were applied in this study.

Evidence-based practice

EBP developed from evidence-based medicine and was first defined as "individual clinical expertise with the best available external clinical evidence" (Sackett, Rosenberg, Gray, Haynes & Richardson, 1996:71). Later, this definition was refined to "the integration of best evidence with clinical expertise and patient values" (Sackett, Strauss, Richardson, Rosenberg & Haynes, 2000:1). According to this refined definition, the following aspects are included during decision making on best practice:

- Research evidence
- Clinical state and circumstances
- Patients' preferences, values and actions
- Clinical expertise

EBP can be seen as circles in which the different aspects involved in EBP are interrelated. Figure 1.1 shows these aspects within the evidence-based model.

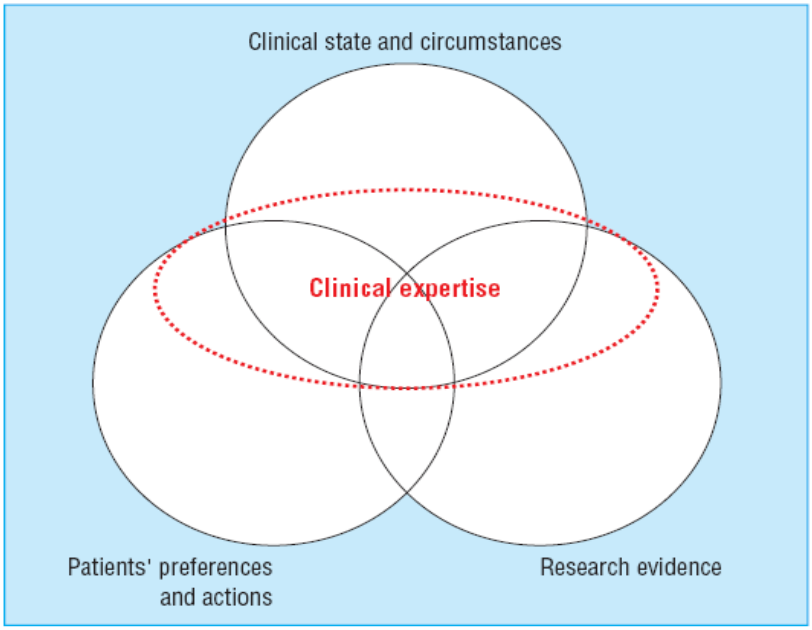

Figure 1.1: Model for evidence-based clinical decisions (Haynes *et al.*, 2002:384)

The aspects in decision making are explained as follows:

Research evidence

Research evidence includes "systematic observations from the laboratory, preliminary pathophysiologic studies in humans and advanced applied clinical research such as RCTs" (Haynes *et al.*, 2002:385). The aim of research evidence should be that it must be applied in practice. Therefore, research findings should be showed in such a manner that practitioners realise its meaning and can decide whether to apply this evidence in daily practice or not (Oermann, Roop, Nordstrom, Galvin & Floyd, 2009:35). Guidelines could help in this process and can be defined as "means for consistent and effective care" (Keeley, 2004:368). In best practice guidelines the recommendations are graded on the basis of the quality of the supporting evidence (Melnyk, 2004:323). Evidence gained from a systematic review can be considered strong due to the systematic review's characteristics of: (1) containing a particular method for the search, and (2) the appraising and (3) synthesising of the outcomes from the primary studies found. This strong evidence can lay the foundation for practice guidelines, which can help to translate research evidence into clinical decision aids, optimise health and patient outcomes and educate clinical practitioners in the health sector by providing the most recent scientific literature (Lam & Kennedy, 2005:167). Therefore, a systematic review could play an important role in EBP and policy and can be utilised in decision making (Dixon-Woods, Bonas, Booth, Jones, Miller, Sutton, Smith, Shaw & Young, 2006:27; Scott, Moga, Barton, Rashiq, Schopflocher, Taenzer & Harstall, 2007:681).

Clinical state and circumstances

The clinical state and the circumstances in which the patient finds herself are important aspects in clinical decision making. For example, when an evidence-based decision should be made concerning the best infant-feeding practice, both the mother's clinical state (e.g. HIV positive) as well as her personal and environmental circumstances (such as the community of which she is part) should be taken into consideration. The decision should fit the HIV-positive mother's personal and environmental circumstances best.

Patients' preferences and actions

EBP is conducted when choices concerning the care of the patients should be made according to all "valid relevant information" (Pearson, 2005:93). This requires the involvement of the patient in the decision-making process to prevent negative ethical results that might be caused when practice is only based on research outcomes (Ingersoll, 2000:151). An ethical result or problem might occur when the patient's preferences are in contradiction to the actions the patient takes. For example: Although the HIV-positive mother is willing to heat-treat her EBM, she might not able to practice it due to fear of rejection by her family. This means that the mother's preferences and actions should always be taken into consideration and respected in the decision making concerning best infant-feeding practice.

Clinical expertise

Clinical expertise includes the clinical practitioner's basic skills together with his/her experience (Haynes *et al.*, 2002:385). It is important to include both the practitioner's basic skills and experience to bring practice and theory closer towards each other (Closs & Cheater, 1999:12; French, 1999:73). Therefore, the practitioner should first know where evidence can be found, for example in journals and bibliographic databases (McKibbon & Marks, 1998**a**:68–70). Secondly, in order to apply the "best available evidence to inform practice", practitioners should have knowledge and understanding of the process with regard to carrying out the research and critiquing it to be able to determine which research evidence is 'best' (O'Mathuna, Fineout-Overholt & Kent, 2008:107). It is furthermore vital that the practitioner knows how to make a decision whereby the best evidence is integrated with the patient's preferences, clinical state and circumstances, and how to provide the patient with the information required to make an informed choice (Forrest & Miller, 2004:347; Haynes *et al.*, 2002:385). For the HIV-positive mother it means that health care workers should know how to interpret what is best for the HIV-positive mother (based on the integration of research evidence, patient preferences, clinical state and clinical expertise) and inform the

mother with best-evidence information in order to make an informed decision regarding an infant-feeding option that suits her and her environment best.

1.5.4 Methodological assumptions

According to Mouton and Marais (1994:7), social research entails the following elements: a *model*, *dimensions* and *determinants*. These elements are explained below.

In this systematic review, the model for nursing research developed by Botes (1992, adapted from Mouton & Marais [1994]) is applied. The model introduces nursing activities in three orders: *practice*, *nursing science* and *paradigmatic perspectives*. Although these orders are explained separately, they are interrelated. The first order entails the *practice* of nursing. This order forms part of the empirical world (reality). Nursing research problems are derived from this empirical world / nursing practice. The focus is on the individual patient. For this study the aim of this order involves improving nursing practice to the benefit of the individual HIV-positive mother and her infant that needs safe infant feeding. The researcher followed a functional approach in research and positioned the study in the second order of nursing activities of Botes's model. The second order is the *nursing science*, which is developed both through research and theory generation. It involves focussing on a model (Botes's model) for research, the dimensions and determinants (which involves certain criteria for doing research). The third order concerns the meta-theoretical assumptions, theoretical assumptions and methodological assumptions. My methodological approach was influenced by my paradigmatic perspective and I endeavoured to ensure that the methods for this research were congruent with my meta-theoretical and theoretical assumptions (see paragraphs 1.5.2 and 1.5.3).

According to this model, both quantitative and qualitative methodologies and types of research can be used (depending on which method fits the research question best). Botes promotes a functional approach. This means that it serves practice and can be utilised in practice. This research was not conducted merely 'for the sake of research', but for a higher goal, namely to serve practice. This systematic review will be valuable for practice by providing valuable recommendations for research, education, policy and practice, which will be made assessable to practitioners by it being published.

Within the research process, several decisions should be made. The researcher approaches the research from his/her belief/worldview or paradigm, which also includes the researcher's reasons to do research in the first place or interest in the research topic (see paragraph

1.5.2). The worldview is interwoven within the theoretical/methodological framework (research strategy and research goal). Beliefs derive from this paradigm, and are referred to as the determinants of the choices made within the research process.

Functional approach

The functional approach implies that the researcher uses the research method most suitable to answer the research question derived from the research problem. An explanation of how the research method serves to answer the research question for this study was provided in paragraphs 1.1 and 1.3).

Figure 1.2 outlines the research process, which includes the determinants and research decisions (the phases or steps that take place throughout the research process).

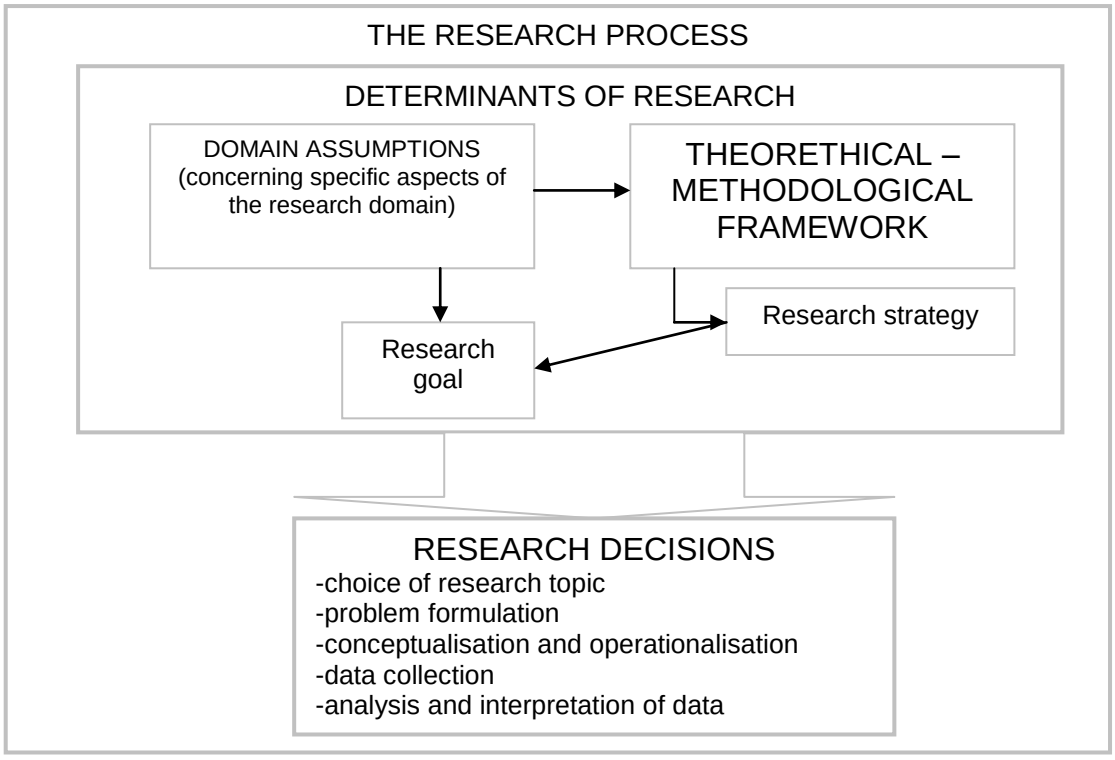

Figure 1.2: The research process, determinants and research decisions (adapted from Mouton & Marais, 1994:22)

Application to my research

Botes urges researchers to take determinants of research into consideration when planning and conducting their studies. An explanation for the determinants considered in this study and how this influenced the study decisions is provided in this section. Firstly, the researcher is committed to conducting research that provides high-quality evidence. This evidence should serve practice by being translated into clinical decisions. The model for evidence-

based clinical decisions, which was chosen as theoretical framework for this study, supports the view of the researcher, namely that it is important to translate evidence into clinical decisions in which the following aspects are included during decision making on best practice: research evidence; clinical state and circumstances; patients' preferences, values and actions; and clinical expertise. Choices are explained and justified throughout the study. The reason for each decision, such as the topic and problem formulation, is provided in the background (see paragraph 1.2) and problem statement (see paragraph 1.3). The research was conducted according to the steps of the systematic review. The conceptualisation of these steps is explained in more detail in Chapter 2, and the operationalisation of these steps is outlined in chapters 3 and 4. The report on data collection is provided in Chapter 3. Operationalisation of the analysis (see Chapter 4) and interpretation are justified and explained (see chapters 4 and 5).

1.6 CLARIFICATION OF TERMINOLOGY

Some concepts used in this study are hereby explained to provide clarity. Table 1.1 clarifies the conceptualisation of the definitions used within this study.

Table 1.1: Conceptualisation

Review question	How effective is heat treatment of EBM as an in-home procedure to inactivate the HI-Virus: a systematic review. This refers to effectiveness in terms of (1) eliminating/inactivating the HI virus and safety in terms of retaining the protective and nutritional value of the EBM; (2) feasibility as an in-home procedure; and (3) acceptability by the mothers and their communities.	
Concepts in the study		
	General/'everyday' definitions Joint Committee on Health Education Terminology, 1973:63; OED, 2009; Pomerleau, 2001:65 (WHO)	**Conceptual definitions**
Effectiveness	Safety: denoting something designed to prevent injury or damage. Feasibility: possible and practical to achieve easily or conveniently (OED, 2009). Acceptability: adequate, though not outstanding or perfect.	Eliminating the HI virus and retaining the protective and nutritional value of EBM after heat treatment. The extent of practicability of heat treatment of EBM as an in-home method. The perception and willingness of HIV-positive mothers with regard to heat treatment of EBM as a method used in the home in their communities.
Heat treatment:	The use of heat for the therapeutic purposes in medicine or to modify the properties of a material, especially in metallurgy (OED, 2009).	Pasteurisation, treating human milk with heat based on comparison of three procedures: Holder pasteurization, flash-heating and Pretoria pasteurisation.

EBM:	Expressed breast milk Refers to milk that has been taken out of the breasts by manual pressure or pumping (Pomerleau, 2001:65).	Manually expressed human milk.
In-home *Procedure:*	(in)-home: the place where people live. Series of actions conducted in a certain manner (OED, 2009)	Heat treatment used by mothers at home.
HIV	Human immunodeficiency virus, the cause of Aids (acquired immune deficiency syndrome) (Pomerleau, 2001:65).	HIV type 1-positive mothers and mothers with unknown HIV status.
Health education	A process with intellectual, physiological, and social dimensions relating to activities which increase the abilities of people to make informed decisions affecting their personal, family and community well-being. This process based on scientific principles facilitates learning and behavioural change in both health personnel and consumers, including children and youth (Joint Committee on Health Education Terminology, 1973:63).	Evidence-based knowledge provided to the HIV-positive mother to increase her ability to make an informed decision regarding safe, feasible and acceptable infant feeding that positively affect the well-being of her infant.

1.7 RESEARCH DESIGN

This study used a descriptive design to critically synthesise, by means of a systematic review, the best available existing evidence and provides a clear overview of the effectiveness of heat treatment of EBM as an in-home procedure to inactivate the HI virus. The systematic review is a helpful method to summarise the best-quality empirical evidence of the benefits and limitations of heat treatment as in-home procedure (Kitchenham, 2004:3) and to provide recommendations for (the refining of) future research (Cook, Mulrow & Haynes, 1997:376, 378). It also offers a summary of the best available evidence to clinical practitioners with limited access to a wide variety of research literature and limited time to read this literature. Such a systematic review can also help to educate and update health workers and increase their ability to translate research evidence into clinical decision aids and thereby optimise health outcomes to practice safe and effective care (Cook, Greenhold *et al.,* 1997:210; Magarey, 2001:381; Sutherland, 2004:47).

This study is a combination of a quantitative and qualitative systematic review. It includes both qualitative and quantitative primary studies in the study sample. The term ‘systematic

review' was chosen instead of 'integrative review', because a systematic review includes only research studies while an integrative review also includes other documents, for example policies and guidelines (Ellis, 1991:233). Therefore, the aim of a systematic review is to combine the evidences of an intervention (Kitchenham, 2004:3), such as heat treatment as an in-home procedure, while the aim of an integrative review is to collect all information on a topic as basis for example, a concept analysis (Pompeo, Rossi & Galvao, 2009:435).

STEPS OF A SYSTEMATIC REVIEW

A research plan in the form of a research protocol/proposal was drafted in order to give evidence of the prospective planning of the methodology (CRD, 2009:15) according to the specific steps of the systematic review, which are outlined in Table 1.2.

Table 1.2: Steps of the systematic review (adapted from ADA, 2008:6–65; Magarey, 2001:377)

Step 1: Formulating a focussed review question.
Step 2: Gathering and classifying the evidence, which include identifying (by searching the literature and selecting studies to be included) relevant studies for inclusion (sampling procedure).
Step 3: Performing the critical appraisal.
Step 4: Summarising the evidence (which includes data extraction and data analysis/synthesis).
Step 5: Drafting the conclusion statements (including conclusions, limitations and recommendations).

A more detailed overview of the methodology and realisation in accordance with the steps of this study is provided in chapters 2 and 3 respectively.

1.8 RIGOUR

Rigour involves the concepts *validity* (both *internal* and *external* validity) and *reliability*. Validity refers to the "measure of truth or accuracy of a claim" (Burns & Grove, 2005:215). Internal validity refers to truth of reality (Burns & Grove, 2005:215), while the term external validity can be related to the ability to generalise and contextualise the findings of the study (Burns & Grove, 2005:218–219).

Reliability refers to the extent of consistency of the measure (Burns & Grove, 2005:749). In case of a systematic review, the 'measure' can be related to the tools used in the critical appraisal (process). These tools should therefore be consistent. Consistency hereby refers to agreement (similarity in outcomes) between different independent reviewers using the

same appraisal tool during the critical appraisal process, which is referred to as interrater-reliability (Burns & Grove, 2005:740).

To increase rigour in all types of reviews (particularly systematic review and meta-analysis), specific issues should be taken into consideration. To increase rigour in a systematic review, the problem and purpose should be clearly stated (Badr, 2007:80). Terminology/concepts used in the review should be systematically defined and the problem stated should be supported by and based on a conceptual and theoretical framework (Bravata, McDonald, Shojania, Sundaram & Owens, 2005:1063). To increase internal validity, the literature search should be clearly described (O'Mathuna *et al.*, 2008:104) and conducted as thoroughly as possible by identification of a complete and unbiased set of relevant studies (Hopewell, Clarke, Lefebvre & Scherer, 2008:3) Two threats to internal validity are (1) publication bias, which entails the possibility that positive results receive priority within publications compared to negative results (Kitchenham, 2004:8); and (2) language bias, which refers to the preference journals give to the English language for publication (O'Mathuna *et al.,* 2008:105), while studies written in other languages that might be important and hallmark studies are not given publication opportunity. To reduce publication bias, 'grey' literature, such as conference papers, should be scanned (Kitchenham, 2004:8). To reduce language bias, a search strategy that includes no limitation concerning language should be conducted (O'Mathuna *et al.,* 2008:105). Decreased internal validity could also be caused by a lack of appropriate tools for critical appraisal (McIntosh, Woolacott & Bagnall, 2004:4; Scott *et al.,* 2007:685). A variety of appraisal tools was used in this study. The criterion that all tools should fit to the type of study was used. Finally, another method to increase internal validity is to update the systematic review by updating the search to ensure that no relevant data have been missed (Shea, Boers, Grimshaw, Hamel & Bouter, 2006).

To increase reliability by preventing inconsistency (which could be caused by a lack of skills of the reviewer to critically asses and interpret the designs/studies) (CRD, 2009:34; Scott *et al.,* 2007:685) and to ensure that only studies that are of high quality will be included, the critical appraisal process should be conducted by both the reviewer and an independent reviewer (Akobeng; 2005:848; Allan, Badenoch, Bexon, Carlsson, Dearness, Mihailova & West, s.a.). Although the reviewers do in essence not take part in the sampling procedure (McGowan & Sampson, 2005:75), a team is essential in conducting systematic reviews because involvement of a minimum of two researchers helps to decrease bias and error (CRD, 2009:4). A team of reviewers is namely able to combine their skills and experiences and 'check' each other throughout all the steps of the conducting of the systematic review.

Finally, conclusions and recommendations should only be derived from the evidence that was found in order to ensure that they are rigorous (Badr, 2007:80). To ensure transparency and repeatability in general (Nind, 2006:188), the entire systematic review (including justification of all decisions made in the search strategy) should be reported (CEBC, 2009:10) and presented as transparently as possible in order to prevent that relevant information is omitted (CRD, 2009:41).

The evaluation of rigour in this study is explained in paragraph 5.3.

1.9 ETHICAL STATEMENT

The researcher is committed to ethical research according to the research mission of North-West University. The researcher adheres to the codes of conduct and ethics (which is supported by the North-West University);

- "[As a student I will] maintain the highest standard of honesty and integrity in obtaining relevant study materials, doing assignments, writing tests and examinations and in presenting my academic and non-academic achievements to any other person(s) throughout my life" – Code of Conduct (Landman, Punt & Painter-Morland, 2002:33).
- "[We commit ourselves] To uphold human dignity in all our activities, undertaken to develop the full potential of others and of ourselves, requiring that we practise and promote accuracy, honesty, truthfulness, trustworthiness and loyalty towards the University and all its people" – Code of Ethics (BESA, s.a.:33).

The chairperson of the Ethics Committee was consulted and indicated that ethical approval was not required before performing a systematic review due to the fact that no human beings are involved as subjects. However, there are some ethical issues that were taken into consideration.

Firstly, it is the researcher's responsibility to carry out research of high quality. Therefore, high standards were maintained concerning planning, implementing and reporting the research (see chapters 3, 4 and 5). Planning, implementation and reporting were conducted as carefully as possible in collaboration with the research committee and supervisors.

Ethics were taken into consideration during the critical appraisal of the studies. Although no crucial cut-off point was used, studies that were not conducted in an ethical way scored lower in terms of general rigour. Furthermore, transparency was ensured through detailed reporting of the decisions made in the selection and obtaining of relevant data.

Secondly, the researcher should be competent and accurate. The researcher should also take auditability into consideration, which refers to the consistency of the decisions the researcher makes at every stage of the research process (Beck, 1993:263).

It is the researcher's responsibility to conduct research in an honest way (Rossouw, 2005:40). Honesty in this study was ensured by upholding integrity through stating both supporting and opposing points of view found in the data. Plagiarism was avoided by giving credit where it is due in the text and including bibliographic details in the list of references. The entire study was conducted as clearly as possible and is an honest reflection of the whole research process (Brink, 2006:30–43).

Thirdly, it is the researcher's responsibility to share the research results (Brink, 2006:30–43; Cummings, 2007). The research results, which were obtained from the systematic review, should be shared with other scientists and the public in an understandable way (Olivier, 2003:17, 19). Therefore, this study will be submitted for publication in a journal in the relevant research field.

1.10 SUMMARY

This chapter provided an overview of the way in which this research was conducted. First, it contained a brief introduction. The background was provided in order to understand the problem statement and need for this systematic review. Then the research question was stated. This chapter also explained the paradigmatic perspective of the researcher and set out the central theoretical argument, the meta-theoretical assumption (which involves the researcher's view of man, society, health and nursing) and the epistemological assumptions. It also provided the theoretical framework based on Haynes *et al*.'s model for evidence-based clinical decisions (2002) and the methodological assumption of the researcher involving a model (Botes's model for nursing research, including the three orders of nursing), dimensions and determinants of nursing research. Furthermore, a theoretical clarification of terminology was given, the systematic review as design was explained, and an explanation of how rigour (validity and reliability) should be ensured in a systematic review was provided. Lastly, the ethical statement was provided. An overview of the systematic review as a research method is outlined in the next chapter.

CHAPTER 2:

The systematic review as research method

2.1 INTRODUCTION

The methodology of the systematic review (according to the specific steps of a systematic review) is explained in this chapter.

2.2 METHODOLOGY

According to Allan *et al*. (s.a.), a systematic review is "a review of a clearly formulated question that uses systematic and explicit methods to identify, select and appraise all of the relevant research, and to collect and analyse data from the included studies". The specific steps of the systematic review therefore involve the following: formulation of a research question, a search for relevant literature, selection of studies to be included, critical appraisal, data extraction and analysis, and synthesising of data (Magarey, 2001:377), followed by the formulation of conclusion statements and contextualisation of these statements (ADA, 2008:59–65).

The purpose of a systematic review is to collect data and identify high-quality relevant studies and to synthesise the findings in such a rigorous and comprehensive way that a comprehensive picture of current best available evidence is provided (Badr, 2007:79).

Systematic reviews can be done for a number of reasons. Synthesised evidence derived from systematic reviews can be effectively utilised for the decision making related to health policy and treatment (Badr, 2007:79) and to teaching and health education by publishing it in an adequate way in journals and on electronic databases (Badgett, O'Keefe & Henderson, 1997:886; Badr, 2007:79; Fox, 2005:120). However, on its own the evidence gleaned from a systematic review cannot change practice. It should be part of a collaborative effort to translate evidence into practice and therefore it should form part of an evidence-based model. The model for evidence-based clinical decisions (Haynes *et al.*, 2002:385) is an example of such a model (see paragraph 1.5.3).

The systematic review can include different types of review, as outlined in Table 2.1.

Table 2.1 Types of systematic review

	Types and definitions	*References*
Quantitative systematic reviews	Meta-analyses (when statistical/quantitative methods are applied and combined whereby each primary study is abstracted, coded and entered into a quantitative database in order to link the outcomes of two or more papers).	Altman, 1999:40–41; Lam & Kennedy, 2005:169; Scholten, Clarke & Hetherington, 2005:S147–S148; Whittemore & Knafl, 2005:547
Qualitative systematic reviews	Meta-ethnography and meta-synthesis, e.g. when qualitative studies with the same area of concern are included.	Flemming, 2007:617
Qualitative and quantitative systematic reviews	Combination of quantitative and qualitative systematic reviews.	Whittemore & Knafl, 2005:547
Systematic reviews also include review articles, integrative publication, practice guidelines, economic evaluations and clinical decision analyses.		Badr, 2007:79; JBIEBNM, 2000:1

2.3 STEPS OF A SYSTEMATIC REVIEW

When a systematic review is chosen as design, a review protocol should be planned in order to indicate prospective planning with regard to the methodology of the study, thereby minimising bias (CRD, 2009:15). Therefore, the protocol should state the specific steps within the process of a systematic review (which are explained below).

As indicated in Table 1.2 in the previous chapter, a systematic review is conducted according to the following steps:

- Step 1: Formulating a focussed review question.
- Step 2: Gathering and classifying the evidence, which include identifying (by searching the literature and selecting studies to be included) relevant studies for inclusion (sampling procedure).
- Step 3: Performing the critical appraisal.
- Step 4: Summarising the evidence (which includes data extraction and data analysis/synthesis).
- Step 5: Drafting the conclusion statements (including conclusions, limitations and recommendations) (ADA, 2008:6–65; Magarey, 2001:377).

An explanation of the steps of a systematic review is provided in the following subparagraphs.

2.3.1 Step 1: Formulating a focussed review question

To be truly unbiased, a systematic review should start with a focussed and well-defined question, using appropriate (systematic) methods, and include all high-quality research (CRD, 2009:16; Hopewell *et al.*, 2008:3; Lundh & Gotzsche, 2008:1). The review question should be specific enough to focus on applicable literature during the search, but also broad enough to "not overly limit the scope of the literature search", and it should furthermore also serve the purpose of the study (ADA, 2008:16–18). A focussed stated question is important to clarify the link between applicable research and the area in which evidence-based knowledge is required for practice (ADA, 2008:6). Systematic reviews should be carried out prospectively and comprehensively, guided by a well-defined review question. A systematic review question must be answerable and searchable and therefore should include the following variables: population of interest (P), interventions (I), comparative interventions (C) and the outcomes (O) to measure the effect and timeframe (T) – known as the PICOT format (ADA, 2008:16, Melnyk & Fineout-Overholt, 2005:30). Therefore, the PICOT format helps to ask the right question, which is required in finding a valid and reliable answer. During the formulation of the review question, the PICOT format also helps to identify search words.

2.3.2 Step 2: Gathering and classifying the evidence

Searching the literature

The development of an effective search strategy is one of the most important steps of the systematic review (O'Mathuna *et al.*, 2008:103) and will most probably be a process of repetition in order to improve the sensitivity and specificity of the search (see paragraph 3.3). The search strategy aims to identify all the best available evidence relevant to the review question (ADA, 2008:19–20). Therefore, the search strategy should be comprehensive and sensitive to improve the credibility of the review, reduce bias and increase the repeatability (CEBC, 2009:2–3; CRD, 2009:19).

Librarians play a crucial role in many stages of the review. Their role involves applying their knowledge based on experience and training and their abilities to the development of systematic reviews (McGowan & Sampson, 2005:75). A librarian should be involved to help with expanding the search (Kitchenham, 2004:7).

Data sources

In identifying the 'sample', multiple sources are used, such as electronic databases, catalogues, grey literature and manual searches. These sources should be used to ensure that both published and unpublished research studies are found (CEBC, 2009:6). Different searches could be combined (CRD, 2009:16; Kitchenham, 2004:8). Electronic databases (e.g. MEDLINE, CINAHL, ProQuest, which contains theses and dissertations, PsychInfo, the Cochrane database for systematic reviews) (Melnyk, 2004:323) could be searched by using a broad combination of keywords to obtain all relevant articles. Each database has its unique focus, which can overlap in the identification of publications. More than one database can identify particular publications, implicating that duplicates must be ruled out later.

The search in the electronic databases is followed by manual searching, which involves scanning the journals that are not available electronically, reference lists from relevant studies and the content of journals, abstracts and other data that are relevant to the research topic in order to serve as a compensation for inaccurate databases (CRD, 2009:17–18). Grey literature, which contains unpublished papers, reports and conference abstracts (CRD, 2009:17–18), can be obtained by contacting the study authors to find out whether the study was been published somewhere else. Internet resources such as Google and Google Scholar can be used in order to ensure that all relevant research studies have been identified (Eysenbach, Tuische & Diepgen, 2001:211).

Documentation

The process of searching must be well documented (Magarey, 1997:378) in order to obtain a comprehensive overview of the search and to ensure transparency and repeatability (CEBC, 2009:5). The record should include full details concerning the information of the databases, the dates of the search, the search strategy and the number of records obtained by every search (CEBC, 2009:5, 21–22).

Selection of studies to be included

The Centre for Reviews and Dissemination (CRD) states that a search could result in a large amount of initial relevant records that might be included in the review (CRD, 2009:23). To ensure that only relevant and unbiased studies are included in the review, the study selection should be explicit and sensitive, which relates to the extent of precision of the search (Burns & Grove, 2006:357), in other words how exact the search was conducted (OED, 2009) and that it was done in a way that minimises the risk of errors. Concepts such as "validity", "comprehensiveness", "efficiency" and "relevance" should be taken into

consideration during study selection (Scott *et al.*, 2007:681). The strategies to ensure validity in a systematic review was explained earlier (see paragraph 1.8).

In order to select only the relevant articles from a large amount of literature obtained from the search, the researcher should state inclusion and exclusion criteria beforehand. These criteria are related to the elements of the research question, such as subject and outcome (Kitchenham, 2004:9). Inclusion criteria could concern the type of study design, because reliability of the results and validity is related to the study design (CRD, 2009:9); language, to avoid the infiltration of language bias, which occurs when only one particularly language is used and publications in other languages are excluded (CRD, 2009:12); and the study population of interest. Exclusion criteria could involve that the review did not answer the research question or address the hypothesis; the study design was not appropriated to the research question; the sample size was not large enough; or a lack of control exists within the study (Greenhalgh, 1997:243).

To ensure sensitivity, to start off, the total number of studies that meet the inclusion criteria of the search strategy should be recorded, although some will be irrelevant. Only studies that do not meet the inclusion criteria and studies duplicated in more that one database or journal should be removed to limit sampling bias (CEBC, 2009:2–3) as “multiple reporting” could result in biased outcomes within the systematic review (CRD, 2009:25).

To ensure specificity, irrelevant studies should be excluded in the next phase. The relevance of some studies can be determined from the title (and abstract if available) but in other cases the decision can only be made after the full text article has been studied.

Documentation of study selection

When decisions concerning the selection of studies are made, record should be kept of these decisions in order to provide an audit trail and to demonstrate transparency. A flowchart could be used, which shows the number of relevant articles after every step of the search. A detailed list of studies that are excluded, as well as reasons for exclusion, should be part of the record throughout the selection process (CRD, 2009:25).

The end product of Step 2 is a list of those studies that are relevant and comply with the selection criteria.

2.3.3 Step 3: Performing the critical appraisal

After final selection, the next step should be an in-depth appraisal of the relevant research to exclude low-quality studies and strengthen the evidence by determining methodological quality and rigour for inclusion in the final sample (CEBC, 2009:4). Critical appraisal is thus the last step of sampling and should be an accurate and true reflection of the best available evidence.

From an epistemological perspective, 'evidence' can be defined in different ways, which will be reflected by the hierarchy a researcher uses.

Evidence could be arranged according to specific study methods used to obtain evidence. Sometimes systematic reviews (Evans, 2003:77) or RCTs (Frymark, Schooling, Mullen, Wheeler-Hegland, Ashford, McCabe, Musson & Hammond, 2009:177) are considered superior while case studies are seen as lowest in the hierarchy of evidence (Evans, 2003:77; Frymark *et al.*, 2009:177). Some research methods provide more valid outcomes compared to other methods. However, a method that might be assessed as superior could for example have high internal validity (which means that it is able to state that the intervention changed the outcome variable) (Melnyk, 2004:323) but low external validity in comparison to a 'less superior' method such as a descriptive study (Evans, 2003:77). Therefore, levels of evidence hierarchies might be helpful.

A hierarchy of evidence provides appraisal of the level of evidence derived from different types of methods included in the systematic review. The level of evidence can be graded as follows:

- Grade I refers to good/strong evidence derived from studies that have a strong design and that answer the research question.
- Grade II refers to fair/medium evidence derived from studies containing a strong design. However, these studies contain inconsistency in results caused by bias, inadequate sample size, etc.
- Grade III is limited/poor evidence provided in studies that have a weak design and fail to answer the research question.
- Grade IV evidence refers to expert opinions, which apply to studies in the conclusion merely contains the statements and the views of experts based on their clinical expertise.
- Grade V evidence is not assignable, which means that evidence is not available to directly support or refute the conclusion. (ADA, 2008:87; Minnie, 2007:191–192)

In addition, grading involves the determination of the extent of *effectiveness* (utilisation of clinical guidelines), *appropriateness* (perception of the receiver of the evidence, e.g. of an intervention) and *feasibility* (environment of implementation of the intervention) (Evans, 2003:77).

The systematic review method is seen as the highest level of evidence by its virtue of excellent extent of *effectiveness*, *appropriateness* and *feasibility* (Evans, 2003:77; McKibbon & Marks, 1998**b**:106). Although this method is seen as the best way to provide evidence of the effectiveness of practice interventions, a range of research designs could be used based on one single condition, namely that the design used should fit the research question (Mulhall, 1998:5–6).

Critical appraisal tools

Different instruments for critical appraisal can be used. It is important to use appropriate instruments that fit the research design to appraise a research study, as this will strengthen its internal validity (Akobeng, 2005:848). The disadvantage of critical appraisal tools is that there is not one single tool that can be fully applied in all reviews (CRD, 2009:44). Therefore, Katrak, Bialocerkowski, Massy-Westropp, Kumar and Grimmer (2004:8) recommend that researchers should decide on tools for critical appraisal based on the existing evidence, which means that the tool will contain a scientific construct and will appraise and interpret evidence in a valid and reliable way.

According to Cummings (2007) and Magarey (1997:379), the critical appraisal should also be executed by a second independent reviewer. The second reviewer should be independent, to enhance a neutral, non-preconceived view during the process of critical appraisal. Independency therefore increases the reliability of the review by limiting selection bias.

Blinding involves withholding the identity of authors of a study from the independent reviewers to reduce reviewer bias, which for example involves favouring certain authors or instructions (Ross, Gross, Desai, Hong, Grant, Daniels, Hachinski, Gibbons, Gardner & Krumholz, 2006:1679), thereby enhancing the objectivity of the critical appraisal (Regehr & Bordage, 2006:834). Disagreement among reviewers is in many cases caused by simple oversights, while in some cases it is due to a difference in interpretation or inexperience of the reviewers. Disagreements should be discussed in order to reach consensus and a final decision should be made to include or exclude the study (CRD, 2009:24).

Documentation of the critical appraisal

The quality appraisal of each of the relevant studies should be documented. In addition, a record should be compiled (in the form of a list) of studies that are excluded throughout the critical appraisal process, and the reasons for exclusion should also be documented. Documentation can be done either electronically or via the traditional 'paper-and-pencil' way (CRD, 2009:25).

The studies that are included after the critical appraisal will serve as the final sample for the next step: summarising the evidence by data extraction and data analysis/synthesis.

2.3.4 Step 4: Summarising the evidence

Summarising the evidence from the selected studies involves a process of data extraction and data analysis/synthesis.

Data extraction

According to the CDR (2009:28), data extraction can be defined as "the process by which researchers obtain the necessary information about study characteristics and findings from the included studies". This means that the data collection for the systematic review is done by the extraction of the relevant research studies from the sample studies. Data extraction allows the researcher to determine which data will be most important in answering the review question. For instance, studies with high quality (high score) will carry more weight in the evidence summary than "medium-quality" studies (ADA, 2008:51–52).

The characteristics and findings of the selected studies must be extracted and presented in carefully designed spreadsheets (CEBC, 2009:12). The report on the data extraction serves as information for reviewers and is helpful in compiling the conclusion. Extraction elements are columns in the table to serve as a basis for analysis of study characteristics, weaknesses and outcomes. These elements depend on the review question. Elements for data extraction could be the following:

- General information (e.g. the researcher performing the study, date of study and publication and identification features of the study, such as the author(s) and publication year).
- Study characteristics:
    - Participant characteristics (e.g. age, gender, ethnicity, socioeconomic status).
    - Intervention and setting (e.g. the setting in which the intervention/research is delivered/conducted and the description of the intervention(s) and control(s)).

- The aim/objectives of the study, study design, study inclusion and exclusion criteria.
- Outcome data/results (e.g. the unit of assessment/analysis – for each outcome this includes the measurement tool or method used, results of study analysis, etc.), the implications for practice and limitations of findings. (ADA, 2008:54; CRD, 2009:30–31; Frymark *et al.,* 2009:178)

Data of whatever is relevant to the review question can be extracted.

How and which data will be extracted are determined according to the type of research question and the types of studies that are assessable. Data of each particular study can be extracted and documented in different ways. It is recommended that before data are categorised, extraction of the data be done as thoroughly as possible to ensure that all data will be saved during the data extraction (CRD, 2009:28–29).

In cases where repetition of the extraction of data is impossible, it is recommended that record is kept of how the extraction was conducted to, among other things, provide transparency (CEBC, 2009:13).

Data analysis/synthesis

Data analysis or synthesis involves, among other things, uniting and summarising the outcomes from the single studies that are added in the systematic review (CRD, 2009:45; Kitchenham, 2004:18). The aims of data synthesis are the combining of outcomes, contemplating the strength of outcomes, investigating the consistency of effects within the studies and identifying studies with inconsistent findings. These aims provide reliable conclusions from the included studies (CRD, 2009:45).

In order to give a summary and interpretation of outcomes and characteristics of the included studies, systematic reviews usually provide both text and tables (CEBC, 2009:16; CRD, 2009:45,48).

After analysing the data, it is recommended that a summary of the evidence be written, which serves as a basis for the next step (ADA, 2009:56).

2.3.5 Step 5: Drafting the conclusion statements, limitations and recommendations

Conclusions

The final step in the systematic review is the writing of the conclusion statements. Conclusions must be clear and based on the reviewed studies. The conclusion provides the reader with the researcher's interpretation of a summary of the evidence (CRD, 2009:81). Conclusions are related to the research question(s) and serve as a reflection on the systematic review per se. The American Dietetic Association (ADA) states that evidence sometimes does not support the review question (which should be taken into account in the conclusion) (ADA, 2008:59). Therefore, an outcome of a systematic review could be the conclusion that a lack of evidence exists to completely answer the review question (CEBC, 2009:19). Researchers should therefore be careful and provide a balanced view when reporting and interpreting the results. Examples of unbalanced reporting include incorrect conceptualisation and one-sided reporting, which means that the reviewer only mentions positive results instead of negative results as well (CRD, 2009:75).

Limitations

Limitations are defined as weaknesses of a study (LoBiondo-Wood & Haber, 2002:495). Two types of limitations can possibly exist, namely (1) *theoretical limitations*, which involve the weakness in a study framework (e.g. an unclearly defined concept in the development of a study framework); and (2) *methodological limitations*, which concern the weakness in study design, sampling, measurement, etc. (Burns & Grove, 2005:39–40). Limitations are threats to the rigour of the study. Weaknesses in systematic reviews could be caused by the inclusion of primary studies of poor quality, or poor rigour of the search (due to incomplete searching) or the appraisal technique (Crowther & Cook, 2007:497).

Recommendations

The CRD states that recommendations concerning policy or practice should only be made when the purpose/scope of the review is to provide these recommendations (CRD, 2009:82). The review question and the type of evidence should be the basis for the recommendations concerning policy, practice and further research. Recommendations or implementations for (further) research should be clearly stated. Recommendations should be specific and based on evidence. Merely stating that "more research is needed" is not appropriate. Recommendations for the future should only be provided when methodological cases in the available studies are identified. Finally, in general, recommendations must be ranged in hierarchical order of importance.

2.4 UPDATING OF SYSTEMATIC REVIEWS

Systematic reviews should be updated continuously as science develops. The aim of updating is that the quality of the systematic review can be improved over time (Shea *et al.*, 2006). The same search strategy should be applied when a systematic review is updated, which means it will not be very time consuming (Laupacis & Straus, 2007:273).

2.5 SUMMARY

This chapter provided an overview of the systematic review as methodology. The systematic review was defined and positioned in the typology of reviews. The systematic review process according to its specific steps was also outlined.

Steps of the systematic review include (1) formulating a focussed review question; (2) gathering and classifying the evidence, which includes identifying (by searching the literature and selecting studies to be included) relevant studies for inclusion (sampling procedure); (3) performing the critical appraisal; (4) summarising the evidence (which includes data extraction and data analysis/synthesis); and (5) drafting the conclusion statements (including conclusions, limitations and recommendations). Chapter 3 provides a detailed account of the realisation of this study according to these steps.

The last section in Chapter 2 concerned the updating of systematic reviews.

CHAPTER 3:

REALISATION AND FINDINGS OF THE RESEARCH

3.1 INTRODUCTION

This chapter provides an overview of the realisation of the systematic review conducted according to three of the five specific steps of the systematic review, namely Step 1: Formulating a focussed review question; Step 2: Identifying relevant studies for inclusion (sampling procedure); and Step 3: Performing the critical appraisal. Step 4, which involves the summarising of the evidence, and the realisation of Step 5, drafting the conclusion statements, are explained in the next two chapters.

3.2 THE REVIEW QUESTION

STEP 1: FORMULATING A FOCUSSED REVIEW QUESTION

The review question was approved, piloted and refined with the assistance of the supervisors. The PICOT (ADA, 2008:16; Melnyk & Fineout-Overholt, 2005:30) format was used to ensure a well-structured review question. For this research, the PICOT format also included the setting (S), as setting is considered important due to the use of heat treatment as possible effective in-home procedure. The components (according to PICOT/PICOTS) of the research question are outlined in Table 3.1.

Table 3.1: Components of research question (PICOTS)

P **Population of interest**	HIV-positive mothers
I **Intervention**	Heat treatment as in-home heat treatment of EBM: -Flash-heating -Pretoria pasteurisation
C **Comparison**	As *compared* to -exclusive breastfeeding; -different methods of heat treatment of EBM; and -mothers living in urban versus rural areas
O **Outcomes**	Operational defined as “effectiveness”: Safety: eliminate HIV and retain the protective and nutritional value Feasibility Acceptability
T **Time span and setting**	During first six months and after six months (weaning period) Time period of studies: studies from 1990 until recent
S **Setting**	In-home

The research question was stated as follows:

How effective is heat treatment of EBM as an in-home procedure in terms of (1) eliminating/inactivating the HI virus and safety in terms of retaining the protective and nutritional value of the EBM; (2) feasibility as an in-home procedure; and (3) acceptability by the mothers and their communities?

3.3 GATHERING AND CLASSIFYING THE EVIDENCE

STEP 2: IDENTIFYING RELEVANT STUDIES FOR INCLUSION (SAMPLING PROCEDURE)

3.3.1 Inclusion and exclusion criteria

The sample included all studies that met the following inclusion criteria*:*

- Research studies related to the effectiveness, safety, feasibility, cost-effectiveness and acceptability of in-home methods to heat-treat EBM to destroy the HI virus.
- Studies published since 1990: The methods of Pretoria pasteurisation and flash-heat treatment were both developed recently (studies found were published from the last 15 years until recently).
- Studies including the languages Afrikaans, English and Dutch: because these are the languages the researcher is proficient in.

The sample excluded all studies that met the following exclusion criteria:

- Studies concerning only the Holder method as heat-treatment procedure. Although Holder pasteurisation is widely used in human milk banks, it cannot be used as an in-home treatment due to requirements such as gauges and timing devices (Israel-Ballard *et al*., 2007:318).
- Irrelevant studies
  a. Studies not specific to breast milk / breastfeeding.
  b. Studies not specific to heat treatment / pasteurisation.
- Non-research reports.
- Duplicate studies.

The aim of the search was to include all studies relevant to the research question. Therefore, at first, a broad search was conducted to ensure that all possible studies were included (*sensitivity*). Thereafter, filtering was done to ensure that all studies included were relevant (*specificity*).

3.3.2 Keywords

A broad combination of keywords was used to search (explore) the literature on the topic. The following combination of keywords was used:

(HIV or Aids) **and** (heat or pasteuri* or steri* or boil*) **and** (milk or breast* or human milk or mother* milk or feeding).

To ensure that no relevant data were missed, the keywords were searched (where applicable) in the categories of *All or Title*, *Abstract* or *Author-Supplied Abstract or Keywords*.

Some databases yielded a lack of (relevant) results when the full combination of keywords was used. Therefore, the researcher sometimes had to use only selected keywords in order to obtain sufficient and relevant results. A table was designed to indicate the specific combination of keywords used in each database (see Appendix 1.1).

3.3.3 Sources

To ensure that the search was unbiased, comprehensive and practical, multiple sources (such as different databases and catalogues) were included to identify all relevant research studies. Both published and unpublished literature, for example grey literature, was searched.

Table 3.2 indicates the sources used to ensure a broad as possible search strategy.

Table 3.2 Sources used in the search strategy

	Electronic databases		*Type of literature included*
International	1.	ProQuest	Theses and dissertations
	2.	EBSCOhost: Academic Search Premier, Cinahl, Health Source: Nursing Academic edition, MasterFILE Premier, MEDLINE, PsychINFO and Africanwide NiPAD	Journal articles
	3.	ScienceDirect	Journal articles
	4.	Cochrane	Systematic reviews of studies

National	1	Nexus (National Research Foundation [NRF]) To conduct the search in this database the librarian – who is an expert in literature searches – was consulted due to the fact that it is a complicated database. However, this database was recommended in order to obtain all relevant research studies.
	2.	SAePublications, Sabinet (including Cement and Concrete, Current & Completed Research, FS Articlefirst, FS WorldCat, ISAP by the National Library of South Africa , Kovsidex, NDLTD (theses and dissertations), North-West University Catalogue, SA Media, SAePublications, SA Cat, SANB, Subsidie, UCTD).
		Studies not published in journals
Manual search		• Searched for grey literature such as conference proceedings, discussion papers, report booklets and unpublished research theses. • Manual search was used to obtain articles from the internet and to scan through references.

3.3.4 Role of the librarian

During the search strategy, an experienced librarian from the Ferdinand Postma Library at North-West University was consulted for overall guidance in the choice of databases and a specific search strategy in Nexus (a national electronically database), due to the fact that this database is not user-friendly yet, was needed in order to obtain all the relevant articles.

3.3.5 Documentation of the search

The entire search was documented. Table 3.3 provides a summary of the results of the search.

Table 3.3 Summary of search

Summary of search	DATABASE	Search	For full text	For appraisal
Electronic databases: ***International***	ScienceDirect	235	1	-
	EBSCOhost	155	24	11
	ProQuest	29	1	1
	Cochrane	8	-	-
National	Sabinet (including SA Catalog: SA Cat)	92	-	-
	Nexus (NRF)	33	-	-
Books: *SAePublications*	SAePublications	6	-	-
Internet	Google	3	2	-
References	Reference search	13	12	2
Total		574	40	14

After the initial search was conducted, the titles and abstracts of the articles were examined, during which process inclusion and exclusion criteria were taken into consideration in order to select all relevant studies related to the review question.

Table 3.4 indicates the articles excluded after reading the abstracts and titles according to the databases used. All the remaining, possibly relevant articles were obtained directly via the databases (such as EBSCOhost). Google and Interlibrary Loan were also used to obtain all possibly relevant articles. Record was kept of the articles that were still unobtainable despite efforts to obtain them in different ways. One author was contacted to obtain the full text of a relevant article on flash-heated breast milk as an infant-feeding option for prevention of HIV transmission. Another author was contacted regarding an article on Pretoria pasteurisation. This article could not be found via the manual search, as it was ongoing research and therefore not published yet. However, the first author could not help because the author “could not remember the study” and the second author did not respond via e-mail correspondence.

Obtained articles and full text articles were read and a decision on inclusion for critical appraisal was made (according to the inclusion/exclusion criteria). All relevant full-text articles (that met the criteria) were selected through the search strategy, although some did not meet the criteria (e.g. using other methods than Pretoria pasteurisation / flash-heating). At a later stage, these irrelevant data and duplication of sources were removed where possible and a record of excluded studies, including reasons for exclusion, was drafted (see Appendix 1.2).

Table 3.5 indicates the articles that could not be obtained.

Table 3.4: Articles excluded, according to databases (including reasons for exclusion)

Level 1 (initial search: databases and manual)									
Total excluded, including reasons									
Source	ScienceDirect	EBSCOhost	Sabinet (including SACatalogus: SA Cat):	Nexus	ProQuest	Cochrane	SAePublications	Reference lists	Google
Reasons for exclusion									
Total initial search (n = 574)	**235**	**155**	**92**	**33**	**29**	**8**	**6**	**13**	**3**
1. Irrelevant studies:								0	0
a. Studies not specific to breast milk / breast feeding	197	66	18	6	14	5	4		
b. Studies not specific to heat treatment / pasteurisation	17	31	4	25	14	3			
2. Non-research reports	20	10	47	0	0	0	2	0	1
3. Duplicate studies	0	23	21	1	0	0	0	0	0
Total excluded (n = 529)	**234**	**130**	**90**	**32**	**28**	**8**	**6**	**0**	**1**

Table 3.5 Unobtainable articles

Articles unobtainable (n = 5)		
No.	**Reference**	**Reason**
1.	Anonymous. 2007. AIDS rises sharply in African officials, flash heating inactivation of HIV in breast milk *AIDSReader* 17(7):336–337. ***Source:*** EBSCOhost	Not obtainable via Interlibrary Loan
2.	Mutasa, K.E. 2007. Determining efficacy of in vitro treatment of naturally HIV-1 infected breast milk by heating and microbicides. M-thesis, Unisa, Pretoria. ***Source:*** Nexus	Not obtainable via Interlibrary Loan
3.	Sibeko,L.N. 2007. Acceptability and feasibility of heat-treated expressed breast milk following exclusive breastfeeding by HIV-1 infected South African women PhD-thesis, Macdonald Campus of McGill University, Montreal, Quebec, Canada. ***Source:*** Sabinet	Not available for free (cost £17,50)
4.	Terpstra, F.G., Rechtman, D.J., Lee, M.L., Hoeij, K.V., Berg, H., Van Engelenberg, F.A. & Van't Wout, A.B. 2007. Antimicrobial and antiviral effect of high-temperature short-time (HTST) pasteurization applied to human milk. *Breastfeed Medicine* 2(1):27–33. ***Source:*** Reference list	Not available for free (cost £17,50)
5.	Vitta, B.S. 2006. Acceptability of flash-heating expressed breast milk for the prevention of pediatric HIV in urban and rural Kenya. M-thesis, Davis, University of California, Davis. ***Source:*** Sabinet	Not available for free (cost £17,50)

3.3.6 Levels/Filters in the search

Filtering during the search process enhances the specification of the sample. To obtain the final sample, the four levels of the search strategy are used. Level 1 involves the initial search and scanning of titles and abstracts in order to select relevant studies/papers. In Level 2, full (-text) copies of all relevant studies/papers are obtained. Level 3 entails reading the obtained full text to include/exclude it for critical appraisal (Step 3 of the systematic review). Level 4 refers to the critical appraisal of (full-text) articles and the articles included for data extraction (part of Step 4 of the systematic review) (the final sample), which is outlined in tables 3.6 and 4.1.

Figure 3.1 outlines the realisation of the search strategy (sample), levels 1, 2 and 3, in the form of a flowchart.

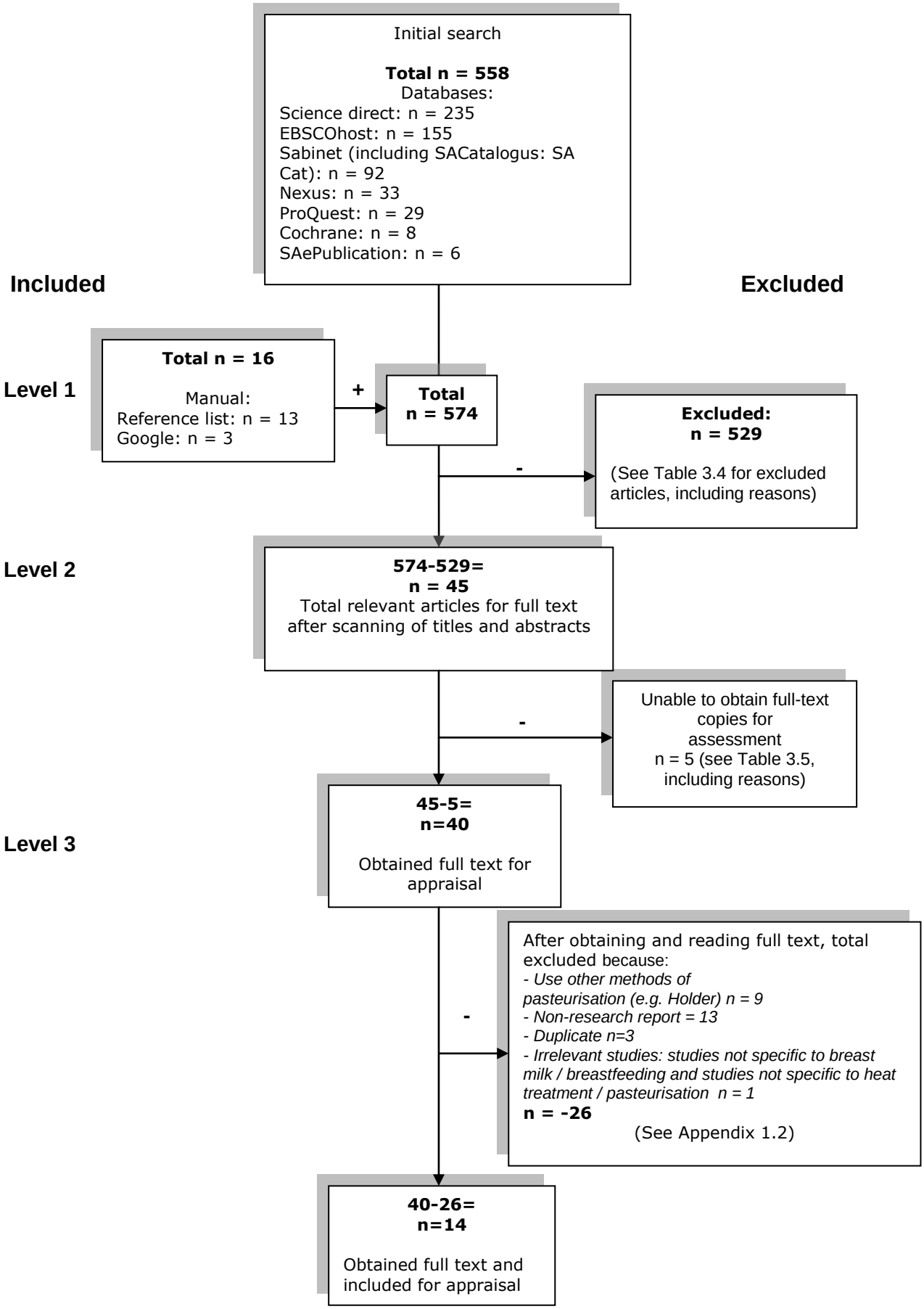

Figure 3.1: Realisation of the search strategy (sample): levels 1, 2 and 3 (CRD, 2009:26)

The last step before critical appraisal can be conducted is classifying the articles according to the type of research design. In order to conduct an appropriate appraisal, the appraisal tool used should fit the design. An appraisal tool that fits the design is also a part of the internal validity (see paragraph 1.8).

3.3.7 Updating the search

To ensure that no relevant data were missed, the entire search was updated six months after the first search by using the same search strategy (including using the same databases, keywords, etc). The second search yielded one relevant study concerning anti-microbiological safety of flash-heat treatment (Chantry, Israel-Ballard, Moldoveanu, Peerson, Coutsoudis, Sibeko & Abrams, 2009), which was included in the critical appraisal, data extraction and finally in the conclusion statement. Updating the search is a method of increasing rigour (see paragraph 1.8).

3.4 QUALITY ASSESSMENT

STEP 3: PERFORMING THE CRITICAL APPRAISAL

Critical appraisal is the last step of sampling to determine methodological quality and rigour for inclusion in the final sample from where data will be extracted. The critical appraisal of the studies is used to evaluate the validity and credibility to determine whether the findings can be considered evidence of 'good methodological quality'. Therefore, objectively structured instruments were used to guide the critical appraisal and reduce the researcher's bias.

The following instruments were used within the critical appraisal process.

- Critical appraisal instrument for reviews (CASP, 2006)
- Critical appraisal instrument for RCTs (CASP, 2006)
- Critical appraisal instrument for cohort studies (CASP, 2006)
- Critical appraisal instrument for qualitative research studies (CASP, 2006)
- The evaluation tool for quantitative research studies (HCPRDU, 2005)
- The critical appraisal guidelines for single case study research (Atkins & Sampson, 2002:107)
- The John Hopkins nursing evidence-based practice (JHNEBP) research evidence appraisal tool (Newhouse, Dearholt, Poe, Pugh & Whithe, 2007:206)

The Critical Appraisal Skills Programme's (CASP) instruments were used as they fit the research design of the samples. The CASP instruments were chosen because they were validated through piloting in workshops, feedback and review of materials (PHRU, 2007). The instruments contain items regarding applicability of the study that is critically appraised, precision and size of the result and validity in general (Mortaz Heijr, 2005). The instruments also largely correspond with other instruments available (Minnie, 2007:165).

The tool from the Health Care Practice Research and Development Unit (HCPRDU) was chosen because it provides a complete overview of the following six sub-sections: (1) study evaluative overview; (2) study, setting and sample; (3) ethics; (4) data collection, analysis and potential researcher bias; (5) policy and practice implications; and (6) other comments (HCPRDU, 2005).

Because both the CASP and the HCPRDU tools do not provide specific tools for single case studies, the critical appraisal guidelines for single case study research, developed by Atkins and Sampson (2002:107), was used, as it was developed specifically for single case studies. This tool is a combination of work by McKay and Marshall (2000:1-11) and Atkins and Sampson (2002:107). It contains 29 open-ended questions in five elements, namely way of thinking; way of controlling; way of working; way of supporting; and way of communicating. The tool was used previously in over a hundred published single case studies in academic and research journals that were part of a pilot study on the use of a systematic review of evidence methodology for information systems research (Wheeler, 2000, cited in Atkins & Sampson, 2002:107).

Finally, the JHNEBP research evidence appraisal tool (Newhouse *et al.,* 2007:206) was used for a study whose design did not fit any of the critical appraisal tools used in this study (De Paoli, Manongi & Klepp, 2003). The JHNEBP tool gauges the strength and quality of recommendations made on the basis of research evidence. The tool contains questions that guide the researcher in determining the level of strength of recommendations and the quality of the primary studies included in the review (Newhouse *et al.*, 2007:99). The tool can be used for both quantitative (experimental, quasi-experimental and non-experimental) and qualitative designs.

The researcher decided in consultation with experienced supervisors that for studies to be called rigorous and thus be included for data extraction, they should obtain a score of at least 6/10 in case CASP was used as a critical appraisal tool during the critical appraisal process. Furthermore, studies were graded according to the definitions, which included

grades I to V, regarding the strength of evidence (ADA, 2008:62, 87, adapted from Greer, Mosser, Logan & Wagstrom Halaas, 2000:700–712), and symbols were used (such as high quality (+), low quality (-), etc.) to provide a quick overview of the quality rate of appraised studies (see paragraph 2.3.3).

Although the conduct of the systematic review was performed by one single researcher, the critical appraisal part was conducted by the reviewer herself and an independent reviewer under the supervision of researchers with experience in the conducting of systematic reviews. Results from both reviewers were compared and a discussion was held to reach consensus in cases of disagreement on the quality of studies and on whether studies should be included or excluded for data extraction. In this study, blinding was not used because there was no conflict of interest. The critical appraisal was conducted by students who did not have interest in the view of experts involved in the field.

Figure 3.2 shows Level 4 (which contains the critical appraisal and data extraction) in the realisation of the search strategy performed within this systematic review to obtain the final sample.

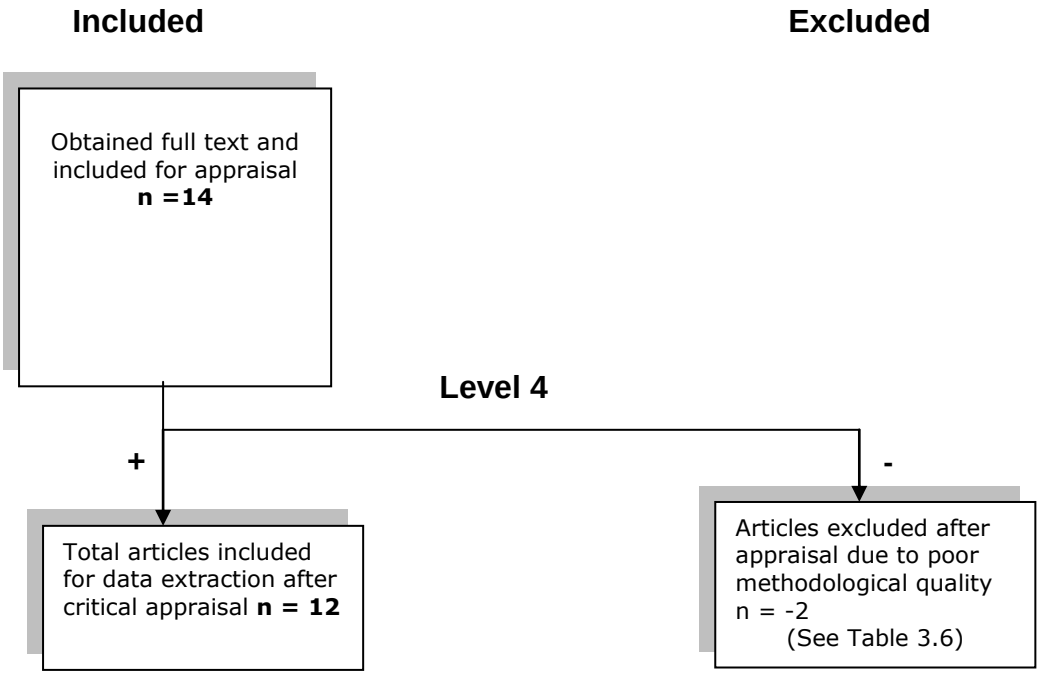

Figure 3.2: Level 4: Performing the critical appraisal (and articles included for data extraction) in the realisation of the search strategy (sample) (CRD, 2009:26)

Table 3.6 shows an overview of the critical appraisal of the studies according to their design.

Table 3.6: Critical appraisal (n = 14)

Included (n = 12)	**RCTs (n = 5)**		
Chantry *et al*. (2009:264–267) Effect of flash-heat treatment on immunoglobulins in breast milk	**Type of study/design** RCT **Setting and intervention** Setting: Laboratory setting, South Africa Intervention: Flash-heating (FH) method	**Research methods** Sample: 50 HIV-positive mothers' EBM (purpose sampling) Data collection: 50 breast milk samples from 50 HIV-positive mothers aliquoted in unheated control and remaining milk samples served as flash-heated (FH) samples. Demographic data collected: Mother: age, BMI, CD4+ count; Infant: age. temperature, immunoglobulin (IgA and immunoglobulin G [IgG]) data and virus data (HIV-1, influenza IgG, IgA, pneumococcal polysaccharide IgA, salmonella lipopolysacharide IgA and poliovirus IgA). Data analysis: Paired t-test on log-transformed data was used for analysis	**Rigour** Instrument used: CASP RCT A clearly focussed question was stated. An appropriate design was applied (including control and study groups). All participants were accounted for in the conclusion. The data collection was done in the same way for both groups. The results were precise and clearly presented. It is unclear whether all important outcomes were considered. It is unclear whether groups were allocated. Follow-up samples were not applicable (samples were breast milk), but it is unclear whether the sample size was large enough and conducted randomly. It is not significant whether blinding was used or not. Overall, the study was fairly planned, executed and reported = medium rigour (7/10) *Grade of evidence:* Grade II **Relevance to the current study** Relevance: + *Antimicrobial safety: Antibacterial and viral safety* Decision: included
Israel-Ballard (2007:1–97)	**Type of study/design** RCT	**Research methods** Sample: 84 HIV-positive mothers provided 75–150 ml manually EBM (purpose sampling) Data collection:	**Rigour** Instrument used: CASP RCT A clearly focussed question was stated. An appropriate design was applied, and the sample was allocated in control and study groups. All the participants were accounted for in the conclusion. The data collection was done in the same way for

Demonstrating the safety of flash-heated breast milk: A potential infant feeding option for HIV positive mothers in developing countries	**Setting and intervention** Setting: Laboratory setting, South Africa Intervention: FH method	**Study 1:** 98 breast milk samples from 84 HIV-positive mothers aliquoted in unheated control and FH samples. Demographic and temperature data were collected. **Study 2:** EBM samples (75–150 ml) collected from 50 HIV-positive mothers aliquoted in unheated control and FH. Data collected concerning temperature and vitamins A, C, B2, B6 and B12 assays. **Study 3:** EBM samples (75–150 ml) collected from 83 HIV-positive mothers. 50 ml of each sample aliquoted in FH, the rest of the sample served as control. Data analysis: **Study 1:** T-test to analyse demographical data from 84 mothers and statistical analyses were performed using Stata 8.0 **Study 2:** Statistical analyses performed using Stata 8.0 **Study 3:** Statistical analyses performed using Stata 8.0	all groups. The results were precise and clearly presented. Although not explicity stated, blinding was probably used. It is unclear whether important outcomes were considered for practice. Follow-up samples were not applicable (samples were breast milk), but it is unclear whether the sample size was large enough and conducted randomly. Overall, the study was well planned, executed and reported = good rigour (8/10) *Grade of evidence:* Grade I **Relevance to the current study** Relevance: + *Virologic safety* (Study 1) *Nutritional safety* (Study 2) *Bacterial safety* (Study 3) Decision: included
Israel-Ballard *et al*. (2005: 175-181) Viral, nutritional and bacterial safety of flash-	**Type of study/design** RCT	**Research methods** Sample: 5 fresh whole breast milk samples (80–120 ml) from healthy lactating women (postpartum 2–12 months) using purposive sampling	**Rigour** Instrument used: CASP RCT A clearly focussed question was stated. An appropriate design was applied, and samples were allocated in control and study groups). All participants were accounted for in the conclusion. The data collection was clear. The results were

heated and Pretoria-pasteurized breastmilk to prevent mother-to-child transmission of HIV in resource-poor countries: A pilot study	**Setting and intervention** Setting: Laboratory setting, Northern California, USA Intervention: Flash-heating and Pretoria pasteurisation (PP) method	inoculated in (1) unheated HIV-spiked milk; (2) flash-heated (FH) HIV-spiked milk; (3) Pretoria pasteurized (PP) HIV-spiked milk; (4) unheated HIV-spiked phosphate-buffered saline (PBS); (5) FH HIV-spiked PBS; (6) PP HIV-spiked PBS; and (7) unheated milk not spiked with HIV Data collection: Pre- and post- (heating) measurements in: *Viral safety:* HIV reverse transcriptase activity (RT) *Nutritional safety:* impact on vitamins A, B6, B12 and C, folate, riboflavin, thiamine *Bacteriologic safety:* antimicrobial proteins (lactoferring and lysozyme) *Storage safety:* amount of *E. coli* or *S. aurus* Data analysis: Nothing mentioned	precise and clearly presented. It is slightly unclear whether important outcomes and results can be applied in practice; however, this was a pilot study, so not applicable. Although not explicit stated probably blinding was used, follow-up samples (sample = breast milk) were not applicable, but it is unclear whether the sample was selected randomly. Unclear how analysis of data was performed. Overall, the study was well planned, executed and reported = good rigour (8/10) *Grade of evidence:* Grade I **Relevance to the current study** Relevance: + *Virologic safety* *Nutritional safety* *Antibacterial safety* *Of both methods (PP/FH)* Decision: included
Jeffery *et al*. (2003: 240–244) The effect of Pretoria pasteurization on bacterial contamination of hand-expressed human breast milk	**Type of study/design** RCT **Setting and intervention** Setting: Laboratory setting, South Africa Intervention: PP method	**Research methods** Sample: EBM samples (30–50 ml) of women (in postnatal ward at a secondary hospital in Pretoria). Total of 58 manually EBM samples divided into 58 control (unheated) and 58 intervention (PP) samples. Data collection:. Pre- and post-measurement. Both groups (PP and unheated) stood up to 12 hours at room temperature. Baseline and temperature data collected at 0 hour, 4 hours, 8 hours and 12 hours. Data analysis: Simple descriptive statistics were used	**Rigour** Instrument used: CASP RCT A clearly focussed question was stated. An appropriate design was applied, and samples were allocated in control and study groups). The data collection was clearly stated. An appropriate sample size was used. The results were precise and clearly presented. Follow-up samples (sample = breast milk) were not applicable. It was unclear how data analysis is done. It was unclear whether important outcomes and results can be applied in practice. Overall, the study was well planned, executed and reported = good rigour (9/10) *Grade of evidence:* Grade I **Relevance to the current study** Relevance: + *Bacterial safety* of PP Decision: included
Jeffery *et al*. (2001:345–349)	**Type of study/design** RCT	**Research methods** Sample: 5 ml of venous blood and 60 ml	**Rigour** Instrument used: CASP RCT

Determination of the effectiveness of inactivation of human immunodeficiency virus by Pretoria pasteurisation	**Setting and intervention** Setting: Laboratory setting, South Africa Intervention: PP method	of manual EBM samples of 51 women (26 HIV-positive women and 25 women with unknown status (between 3 days and 3 weeks postpartum) recruited from the postnatal ward at Kalafong Hospital, Pretoria, using purposive sampling. Each sample was divided into two portions: control and treatment. Data collection: Each sample was measured weekly for p24-antigen, cell-free HIV RNA and integrated DNA. The mean serum viral load of both groups was collected. Data analysis: Numerical methods used	A clearly focussed question was stated. An appropriate design was applied, and samples were allocated in control and study groups. All participants were accounted for in the conclusion). The data collection was clearly stated. The results were precise and clearly presented. Blinding was probably used. Follow-up samples (blood and breast milk) were not applicable. It is unclear whether important outcomes and results can be applied in practice. Overall, the study was fairly planned, executed and reported = medium rigour (7/10) *Grade of evidence:* Grade II **Relevance to the current study** Relevance: + *Virologic safety* of PP (to inactivate HIV in both naturally and artificially infected breast milk) Decision: included
Cohort study (n = 1)			
Coutsoudis (2005:956–959) Infant feeding dilemmas created by HIV: South African experiences	**Type of study/design** Cohort study **Setting** Setting: Cato Manor, Durban, South Africa. Tests in a laboratory setting.	**Research methods** Sample: 315 HIV-positive mothers using convenience sampling Data collection: Biophysical data collected: *HIV-positive mothers:* Blood samples of 315 HIV-positive mothers and breast health data were collected (6, 10, 14 weeks and 9, 12, 15 months) *Infants of these mothers*: Blood samples taken for HIV testing (Polymerase Chain Reaction (PCR) testing: 6 weeks, 9, 12, 15 months enzyme immunoassay (EIA) and p24 testing: 9, 12, 15 months). Infants were weighed, morbidity and feeding data were collected (6, 10, 14 weeks and 9, 12, 15 months). Data analysis: Probably statistical; however, nothing mentioned	**Rigour** Instrument used: CASP cohort study quality The study contained a clearly focussed question. The cohort and outcome were accurately measured to reduce bias. The follow-up was sufficient. The results were clear, precise and believable, and can be applied to the local population and agrees with other available evidence. It is questionable whether the measurement used was appropriate to answer the question (critical note: qualitative methods can be used to gain understanding of feeding practices, which was the intentional goal) and whether the authors identified all important compounding factors. Overall, the study was fairly well planned, executed and reported = medium-good rigour (9/12) *Grade of evidence:* Grade II **Relevance to the current study** Relevance: +/- *Feasibility* and *acceptability* of heat treatment (although other infant-feeding options mentioned) Decision: included

Mixed-method study (n = 1)			
De Paoli *et al*. (2003:611–619) Are infant feeding options that are recommended for mothers with HIV acceptable, feasible, affordable, sustainable and safe? Pregnant women's perspectives	**Type of study/design** Qualitative study using mixed methods: structured interview survey and focus group discussions (FGDs) **Setting** Antenatal clinics in urban and rural districts of Moshi, Tanzania	**Research methods** Sample: -Sample 1: By purposive sampling 500 of 503 (99.4%) pregnant women participated in an interview during their antenatal visits -Sample 2: 46 pregnant women from selected antenatal clinics recruited using purposive sampling Data collection: -Data-collection sample 1: survey: pretested, structured questionnaire including (1) demographic factors; (2) previous infant-feeding experience and knowledge of breastfeeding issues; (3) HIV/Aids- and MTCT-related knowledge; and (4) perceptions of recommendations in revised WHO guidelines. Further self-efficacy of the women was assessed by including questions measured on a scale ranging from 0 (low self-efficacy) to 4 (high self-efficacy) (total of six self-efficacy scales). -Data-collection sample 2: 6 FGDs (with 46 participants) to complement and validate the survey results Data analysis: For all statistical analyses SPSS 11.0 was used (assessed for internal consistency and reliability) FGDs: Tape-recorded, transcribed and coded in themes according to qualitative program (Open Code)	**Rigour** Instrument used: The JHNEBP research evidence appraisal tool (Newhouse *et al.,* 2007:206). The study was clear concerning the recruitment of the sample (sample size was adequate). An adequate description of data-collection methods was provided. The conclusion was based on clearly presented results. Limitations were discussed. Findings were clearly stated. Recommendations particularly for policy and practice guidelines were not clearly stated. Overall, the study was well planned, executed and reported = good rigour. *Grade of evidence:* Grade IV **Relevance to the current study** Relevance: +/- + *Acceptability* of heat treatment. However, it was unclear which heat-treatment method (PP/FH) was mentioned Decision: included
Qualitative studies (n = 4)			
Burke (2004:415–425) Infant HIV infection: Acceptability of preventive strategies in central Tanzania	**Type of study/design** Qualitative study: Exploratory/descriptive design using FGDs	**Research methods** Sample: 12 health workers using a purposive snowball sampling, and five community groups recruited by group letter using purposive sampling	**Rigour** Instrument used: CASP qualitative study The study had a clearly focussed aim. An appropriate qualitative methodology was used. An appropriate research design was used to address the aims of the research. It is unclear whether the recruitment strategy was appropriate to the aims of the research. The data was collected in a way that addressed the research issue

	Setting Semiarid region of Dodoma in central Tanzania	Data collection: Qualitative in-depth interviews (12 health workers) and FGDs (community groups) Data analysis: Qualitative, using coding according to concepts followed by searching for relationships, conditions, results, similarities and differences	and data analysis was sufficiently rigorous. The relationship between researcher and participants was not clearly stated. It is unclear which ethical issues have been taken into consideration. Representativeness was not ensured. In general, findings were clearly stated and the research showed its value for further research and recommendations. Overall, the study was poorly planned, executed and reported = limited/poor rigour (6/10). *Grade of evidence:* Grade III **Relevance to the current study** Relevance: +/- The *feasibility* and *acceptability* of heat treatment; however, not complete study concerning heat treatment, also other infant-feeding options mentioned) Decision: included (although results will weigh less than the medium and strong/good rigour studies)
Israel-Ballard *et al*. (2006:48–60) Acceptability of heat treating breast milk to prevent mother-to-child transmission of human immunodeficiency virus in Zimbabwe: A qualitative study	**Type of study/design** Qualitative study Using FGDs **Setting** 3 geographic regions in Zimbabwe: (1) Harare (urban); (2) Glenview (suburban); and (3) Chipingwe (rural)	**Research methods** Sample: 77 participants recruited by local health care or community centre workers (using purposive sampling) allocated into 4 homogeneous groups: (1) women of childbearing age with breastfeeding experience; (2) grandmothers (> 45 years of age); (3) registered nurse midwives / traditional birth attendants; and (4) fathers of children younger than 5 years. Plus 1 group of HIV-positive women (in Glenview). Data collection: 13 FGDs (4–7 participants) Data analysis: FGD data were analysed using a standard content analysis method according to analytical categories. Coding was done independently by two investigators.	**Rigour** Instrument used: CASP qualitative study The study addressed a clearly statement. The authors used an appropriate method for data collection. The design was appropriate. The analysis was sufficient to answer the research question. The statement of findings was clear. Ethical issues were taken into consideration. It was unclear how the participants were recruited. The relation between researcher and participants was unclear. Overall, the study was well planned, executed and reported = good rigour (8/10). *Grade of evidence:* Grade I **Relevance to the current study** Relevance: + The *feasibility* and *acceptability* of heat treatment (FH) Decision: included

Leshabari et al. *(2006:1–14)* Translating global recommendations on HIV and infant feeding to the local context: The development of culturally sensitive counselling tools in the Kilimanjaro region: Tanzania	**Type of study/design** Qualitative study: Formative research using a combination of qualitative methods (interviews, FGDs and observations) **Setting** PMTCT clinic at the Kilimanjaro Christian Medical Centre (KCMC) and two wards in Moshi district (Moshi town and rural outskirts), Kilimanjaro, Northern Tanzania	**Research methods** Sample: Sample 1: Network sampling: With the assistance of community leaders, key informants: traditional birth attendants, community elders, members of community health committees and nurse counsellors Sample 2: 'Ordinary 'community members in two wards in Moshi district were recruited Sample size: Not mentioned Data collection: -Sample 1: 15 interviews -Sample 2: 8 FGDs (each with 8–12 participants) -Observations Data analysis: Thematic content analysis (reading and re-reading the field notes and transcribed texts, manual coding in the margins and synthesising and grouping data in relatively exhaustive categories).	**Rigour** Instrument used: CASP qualitative study The study addressed a clear statement. The authors used an appropriate method for data collection. The design was appropriate. Sufficient analysis was done to answer the research question. The statement of findings was clear. Ethical issues were taken into consideration. It was quite clear how the participants were recruited It was unclear how big the sample size is. The relation between researcher and participants was unclear. Overall, the study was well planned, executed and reported = good rigour (8/10). *Grade of evidence:* Grade IV **Relevance to the current study** Relevance: +/- The *feasibility* and *acceptability* of heat treatment; however, it was unclear which method (PP/FH)) of heat treatment was mentioned in the study Decision: included
Pullen, A.E., Mokhondo & Jeffery (2002) Attitudes of HIV infected mothers towards expressed and	**Type of study/design** Qualitative study Using individual interviews (open-ended questions)	**Research methods** Sample: 10 HIV-positive women post delivery (including mothers of high-risk, low birth weight infants) recruited using purposive sampling Data collection: Each participant was individual interviewed. A qualitative	**Rigour** Instrument used: CASP qualitative study The study had a clearly focussed aim. An appropriate qualitative methodology was used. An appropriate research design was used to address the aims of the research. The recruitment strategy was appropriate to the aims of the research. The data were collected in a way that addressed the research issue. Ethical issues were taken into consideration. In general the findings were clearly stated and the

pasteurized breast milk for infant feeding	**Setting** Neonatal intensive (NICU) and high-care units (NHCU) at Kalafong Hospital, Pretoria (South Africa)	method in the form of a structured open-ended interview was used. Data analysis: Audiotaped and transcribed verbatim. Technique of text analysis used, including a deductive and inductive strategy.	research showed its value for further research and recommendations concerning health education. It was unclear what the relationship between researcher and participants was. It was unclear whether data analysis was sufficiently rigorous. Overall, the study was well planned, executed and reported = good rigour (8/10). *Grade of evidence:* Grade I **Relevance to the current study** Relevance: + The *feasibility* and *acceptability* of pasteurisation (Pretoria) of breast milk. Critical note: small sample size (n = 10) Decision: included
Experimental studies (n = 2)			
Jeffery & Mercer (2000:219–223) Pretoria pasteurization: A potential method for the reduction of postnatal mother to child transmission of the human immunodeficiency virus	**Type of study/design** Experimental design using pre- and post-repeated measures **Setting** Laboratory setting, South Africa	**Research methods** Sample: Cow's milk , 50–150 ml (purposive) Data collection: Data concerning temperature (initial and ambient) of cow's milk samples (10 times repeated) Data analysis: Lab statistics	**Rigour** Instrument used: Evaluation tool for quantitative research studies (HCPRDU) The aim was clearly stated. The relationship of the study with the area of the review topic was clear. The sample selection (size) was unclear. The analysis was unclear. Group comparison was unclear. The validity of measurement was not totally clear (it was only mentioned that it was precise). Policy and practice implications could not be provided because further research was required. Overall, the study was fairly planned, executed and reported = medium rigour. *Grade of evidence:* Grade II **Relevance to the current study** Relevance: +/- *Safety* (reliability) of PP under a range of conditions; however, no wide range of conditions (as desired) could be tested due to environmental factors Decision: included

Excluded (n=2)			
Reference Yeo, Béquet, Ekouévi & Krawinkel (2002) Attitudes towards exclusive breastfeeding and other infant feeding options: A study from Abidjan, Côte d'Ivoire	**Type of study/design** Quantitative study using experimental cross-sectional (descriptive) design (structured questionnaire survey) **Setting** Three health centres in Abidjan, Côte d'Ivoire	**Research methods** Sample: 150 mothers and 60 pregnant women attended the centres for prenatal consultation, weighing or vaccinating their children using purposive sampling Data collection: Interviews using a structured questionnaire including open or semi-open questions. Data were collected on socioeconomic characteristics of the women's households, knowledge of breastfeeding and exclusive breastfeeding (EBF), attitudes towards EBF and acceptance of alternatives to breastfeeding in case of a transmissible disease by the mother. Data analysis: The data were recorded with Epi-Info Version 6.0 and analysed using SPSS for Windows, Version 10.0	**Rigour** Instrument used: Evaluation tool for quantitative research studies (HCPRDU) The measurement was clear. The sample used was clearly stated and the type of study was clear. It was unclear whether an appropriate design was used to answer the research question of this study. Nothing was mentioned concerning ethics. It was unclear how participants were recruited. It was unclear why there was comparison of pregnant women and mothers within socioeconomic data and later on no comparison between the groups relating to the attitude towards / perception of and knowledge of EBM and attitudes towards other feeding options. Overall, the study was poorly planned, executed and reported = poor/limited rigour. *Grade of evidence:* Grade III **Relevance to the current study** Relevance: - Not a complete study on heat treatment. Not clear what type of heat treatment (PP/FH) is mentioned. Decision: excluded
Case report studies (n = 1)			
Reference Giles & Mijch (2005:237–240) Breastmilk pasteurization in developed countries to reduce HIV transmission: Do the benefits outweigh the risks?	**Type of study/design** Case report **Setting** Australia	**Research methods** Sample: 1 HIV-positive 34-year-old woman Data collection: CD4+ count (collected in the period of 1997–2002) and HIV RNA in breast milk Data analysis: 2 paired specimens of breast milk before and after pasteurisation using ULTRA PRC (post-pasteurisation)	**Rigour** Instrument used: Atkins and Sampson's critical guidelines for single case studies The question was clearly stated. The perspective of the author was mentioned in the discussion. The study provided issues for future research. It was unclear why this study was conducted. It was unclear how the controlling was done (e.g. recruiting unclear, theoretical framework unclear, relevant literature used unclear). The aims and objectives of the study were unclear. The collection and analysis of data were not clearly described / in full detail. Limitations were not mentioned. No logical rigour was mentioned. Overall the study was poorly planned, executed and reported = poor/limited rigour (7/29). *Grade of evidence:* Grade III **Relevance to the current study** Relevance: - Heat treatment was not used from the start. Study was unclear concerning safety, feasibility and acceptability Decision: excluded

3.5 Summary

This chapter provided an overview of the realisation of this systematic review according to three of the five specific steps of the systematic review, which was the following:

Step 1: Formulating a focused review question. The question used was explained according to the PICOTS format.

Step 2: Gathering and classifying the evidence, which included identifying relevant studies for inclusion (sampling procedure). The selection of studies was explained according to the following: inclusion/exclusion criteria, keywords, sources used (which is explained in the text and outlined in a table), and the role of the librarian. Tables were used to outline the articles that were excluded during the initial search according to the databases and reasons for exclusion were provided, as well as the full-text copies that were unobtainable. The documentation of the search was explained and outlined in a table. Furthermore, the realisation of the search and updating of the search was discussed.

Step 3: Performing the critical appraisal (including the critical appraisal tools used). The method of appraisal was explained in the text and outlined in a flowchart and a table.

Explanation of the summarising of the evidence (Step 4) and the realisation of the fifth step, drafting the conclusion statements, is provided in the next two chapters.

CHAPTER 4:

FINDINGS OF THE STUDY

4.1 INTRODUCTION

In this chapter, the realisation of the data extraction (including characteristics of the final sample) and data synthesis (including a summary of the findings and statements regarding the evidence) according to the steps of a systematic review are explained.

4.2 SUMMARISING THE EVIDENCE

STEP 4: DATA EXTRACTION AND SYNTHESIS

Before the details on the data extraction and data synthesis (analysis) are provided, the characteristics of the final sample are explained.

4.2.1 Characteristics of the final sample

In this systematic review, five RCTs were found, of which three can be classified as Grade I: good/strong evidence (Israel-Ballard, 2007; Israel-Ballard *et al.*, 2005; Jeffery *et al.,* 2003) and two as Grade II: fair/medium evidence (Chantry *et al.*, 2009; Jeffery *et al.*, 2001). One cohort study was identified and classified as Grade II: fair/medium evidence (Coutsoudis, 2005). One study using mixed methods was found, of which the evidence was classified as Grade IV: expert opinion (De Paoli *et al.*, 2003). Four qualitative studies were identified, of which two were classified as Grade I: good/strong evidence (Israel-Ballard *et al.*, 2006; Pullen *et al.*, 2002), one was classified as Grade III: poor/limited evidence (Burke, 2004) and one was classified as Grade IV: expert opinion (Leshabari *et al.*, 2006). One experimental study was found, which was classified as Grade II: fair/medium evidence (Jeffery & Mercer, 2000) (see Table 3.6).

The studies concerning safety of heat treatment included the five RCTs (Chantry *et al.*, 2009; Israel-Ballard, 2007; Israel-Ballard *et al.*, 2005; Jeffery *et al.,* 2003; Jeffery *et al.*, 2001; Jeffery *et al.,* 2003) and the experimental study (Jeffery & Mercer, 2000). Information regarding acceptability of heat treatment only was found in the mixed-method study (De Paoli *et al.*, 2003). Both acceptability and feasibility of heat treatment were mentioned in the cohort study (Coutsoudis, 2005) and in all four qualitative studies (Burke, 2004; Israel-Ballard *et al.*, 2006; Leshabari *et al.*, 2006; Pullen *et al.*, 2002).

4.2.2 Data extraction

After selection of the final studies (sample), the selection of the data (findings) from the studies was done. The characteristics and findings of the selected studies were extracted and presented in table format. By providing an overview in table format of the studies from which data were extracted, a quick comparison of studies was possible (ADA, 2008:52).

Data-extraction elements of each study involved the focus of the study, the main findings and findings that were relevant to this systematic review.

Table 4.1 provides information on the data extraction of the included studies (final sample) according to the respective study designs.

Table 4.1 Data extraction (n = 12)

RCTs (n = 5)			
Reference Chantry, *et al*. (2009:264–267) Effect of flash-heat treatment on immunoglobulins in breast milk	**Focus of the study** To evaluate the effect of FH on breast milk immunoglobulin levels and antigen-binding capacity	**Bottom-line findings** *Effect on immunological characteristics:* FH significantly decreased total IgA and IgG concentrations (SD: 318.0 (1.9) vs. 398.2 (1.9) µg/ml and 89.1 (2.7) vs. 133.3 (2.5) µg/ml, $p < 0.001$ each). Although the latter was most affected, FH retained 66% of the antigen-binding capacity. The binding capacity of IgA and IgG to influenza increased after FH ($p = 0.029$ and 0.025, respectively). Therefore, FH is able to retain most of the immunological value of the milk.	**Findings relevant to this study** Findings from this study regarding *safety* of FH: FH is able to retain most of the immunological value of the milk.
Reference Israel-Ballard (2007:1–97) Demonstrating the safety of flash-heated breast milk: A potential infant feeding option for HIV positive mothers in developing countries	**Focus of the study** To determine the *safety* of flash-heat pasteurisation to use as method for HIV-positive mothers in resource-poor countries	**Bottom-line findings** *Virologic safety:* All flash-heated samples showed undetectable levels of cell-free HIV-1 compared to unheated samples ($p < 0.00001$). Therefore, it is effective in eliminating the HI virus. *Nutritional safety:* Vitamin A was not significantly impacted by flash heat treatment, while vitamins B12 and folate increased significantly and ascorbic acid borderline also. Riboflavin and vitamin B6 decreased significantly, retaining 59% and 96%, respectively, of original values. Therefore, FH is safe to retain most of the nutritional value. *Bacterial safety:* Unheated samples had a significantly higher rate of bacterial propagation, including pathogenic growth, over eight hours than flash-heated samples ($p < 0.005$). Therefore, FH is safe to limit bacterial growth.	**Findings relevant to this study** Findings from this study regarding *safety* of FH: FH is able to eliminate HIV, retain most of the nutritional value and limit bacterial growth.
Reference Israel-Ballard *et al*. (2005:175–181) Viral, nutritional and bacterial safety of flash-heated and Pretoria-pasteurized breastmilk to prevent mother-to-child transmission of HIV in resource-poor countries: A pilot study	**Focus of the study** To investigate and compare the virologic, nutritional and antibacterial *safety* of FH and PP by means of a pilot study	**Bottom-line findings** *Virologic safety*: Both methods (FH and PP) inactivated more than three logs of HIV-1. FH resulted in undetectable reverse transcriptase (RT) activity. *Nutritional safety:* Neither method caused significant decrease in any vitamins, although slight reductions in vitamins C (FH by 21% [SD = 47] and PP by 32% [SD = 42]) and E (FH by 10% [SD = 67] and PP by 20% [SD = 43) were noted. *Antibacterial safety:* Heat decreased immuno-reactive lactoferrin ($p < 0.05$) but not the proportions of lactoferrin and lysozyme surviving digestion. FH seems to retain more antibacterial activity. Both treatments eliminated spiked bacteria. Therefore, both methods are able to eliminate HIV, while retaining the nutritional and protective value.	**Findings relevant to this study** Findings from this study regarding *safety* of both methods (PP/FH): Both methods are able to eliminate HIV, while retaining the nutritional and protective value. (This is the only study found where safety of both methods was compared.)

Reference	Focus of the study	Bottom-line findings	Findings relevant to this study
Jeffery *et al*. (2003:240–244) The effect of Pretoria pasteurization on bacterial contamination of hand-expressed human breastmilk	To determine the effect of PP on commensally and pathogenic bacteria in hand-expressed human breast milk, and to determine the duration of time for which milk can safely be kept without refrigeration after PP	*Antibacterial safety:* Bacterial growth: -Control sample: 34 (59%) of the 58 control portions showed bacterial growth, while 4 (6.8%) of the 58 PP treatment portions showed bacterial growth (p = 0.0000, OR 0.0523, confidence interval [CI] 0.01389–0.178523). *Antibacterial safety over time:* After 12 hours, remaining sterile: -Control sample: 5 of 58 control samples remained sterile after 12 hours -PP treatment sample: 53 of the 58 treatment samples remained sterile after 12 hours (p = 0.0000 OR 0.0089, CI 0.001861–0.0373). *Quantity in bacterial growth:* - Control samples: 21 of the 34 control samples had significant bacterial growth, while in the PP treatment sample, 4 of the 34 pasteurised samples had significant bacterial growth (all contained more than one pathogen). Therefore, the PP method is able to retain most of the protective value (over time) and limit bacterial growth.	Findings from this study regarding bacterial *safety* of PP: The PP method is able to retain most of the protective value (over time) and limit bacterial growth.
Reference	**Focus of the study**	**Bottom-line findings**	**Findings relevant to this study**
Jeffery *et al*. (2001:345–349) Determination of the effectiveness of inactivation of human immunodeficiency virus by Pretoria pasteurisation	To determine whether PP effectively *inactivates* HIV in human milk	*Virologic safety (viral replication):* 1. Samples from HIV-positive women (naturally infected breast milk): -Control sample: 5 of the 26 showed evidence of viral replication. -PP treatment sample: None of the 26 showed evidence of viral replication. 2. Spiked samples from women of HIV-negative or unknown status (artificially infected breast milk): -Control sample: 4 of the 25 showed evidence of viral replication. -PP treatment sample: None of the 25 showed evidence of viral replication. No pasteurised sample showed any increase in RNA viral load. Therefore, the PP method is able to effectively inactivate HIV in human milk.	Findings of the virology *safety* of PP: The PP method is able to effectively inactivate HIV in human milk.
Cohort studies (n = 1)			
Reference	**Focus of the study**	**Bottom-line findings**	**Findings relevant to this study**
Coutsoudis (2005:956–959) Infant feeding dilemmas created by HIV: South African experiences	To highlight the dilemma created by the risks and the benefits of breastfeeding, to discuss the implementation in South Africa of the Safer Breastfeeding Programme, to reduce	Of 188 infants tested for HIV, 4 (2.6%) tested positive at nine months of age. The risk of transmission was more or less 0.35% per month of breastfeeding. *Breast pathology:* Of 188 mothers (remained in follow-up for nine months), breast pathology occurred in 179 mothers who had been breastfeeding. Cracked nipples was experienced by 21 (12%) of the mothers. Mastitis was diagnosed in only 4 (2%) of the mothers. Therefore, it is important to take breast pathology into consideration in follow-up visits. *Early cessation of breastfeeding:* 56 mothers had stopped breast feeding between six and nine months. A total of 89.3% experienced problems. Emotional distress experienced by the mother was the most common problem. One of the most common	Findings from this study regarding *feasibility* and *acceptability* of heat treatment: Heat treatment was not seen as feasible (too time consuming) and not well accepted (mainly due to a lack of knowledge of the method and lack of confidence, stigma and other alternative methods already being available).

	some of the known risk factors (e.g. breast pathology) associated with HIV transmission and to highlight some infant-feeding options (use of early cessation of breastfeeding and heat treatment of EBM)	strategies used to discontinue breastfeeding between six and nine months is EBM, followed by applying chillies or aloes to put the child off the breast, sending the child away or the mother sleeping apart from the baby. *Heat treatment of EBM:* From 148 infants, 9 (6%) received heat-treated EBM (HTEBM). Counsellors were surprised by the low uptake of heat treatment due to: 1) it not being officially endorsed by the Department of Health; 2) it being felt that a reduced amount of milk is expressed and the baby would not be satisfied; 3) the baby still demanding the breast after feeding, probably for reasons of comfort/contact; 4) a lack of confidence in the procedure because mothers did not have the opportunity to see a demonstration of the method; 5) it being regarded as stigmatising, possibility of being associated with witchcraft, or time consuming; and 6) formula being readily available as an alternative.	
Mixed-method studies (n = 1)			
Reference	**Focus of the study**	**Bottom-line findings**	**Findings relevant to this study**
De Paoli *et al*. (2003:611–619) Are infant feeding options that are recommended for mothers with HIV acceptable, feasible, affordable, sustainable and safe? Pregnant women's perspectives	To investigate pregnant women's views on infant-feeding options recommended for HIV-infected women	Participating women reported that they would change to an alternative infant-feeding method if they were found to be HIV infected and were advised to do so. *Cow's milk* was regarded as the most feasible infant-feeding method for local HIV-infected mothers. *Infant-feeding formula* was regarded as too costly, but if recommended by health workers and distributed free of charge, the majority of the women (82%) were confident that they would then choose this option. *Exclusive breast milk:* Women were less optimistic and expressed great concern about the social consequences of not breastfeeding. The safety of exclusive breast feeding (EBF) was questioned. *HTEBM and wet-nursing* were not regarded as viable options. Several social barriers were identified, including a possible lack of support from the partner and potential negative reactions from the community (fear of stigma/rejection).	Findings from this study regarding *acceptability* of heat treatment: Heat treatment was not well accepted due to social barriers such as lack of support and fear of stigma.
Qualitative studies (n = 4)			
Reference	**Focus of the study**	**Bottom-line findings**	**Findings relevant to this study**
Burke (2004:415–425) Infant HIV infection: Acceptability of preventive strategies in central Tanzania	To explore factors that may influence the *acceptability* of the following infant-feeding interventions: nevirapine treatment, replacement feeding, EBF and heat-treating breast milk	*Limitations* to future adoption of infant-feeding options are resource limitations, stigma of HIV/Aids, widespread fear of HIV-testing, and insufficient education. *Acceptability* of the following infant-feeding options: *-Nevirapine* would be well excepted, especially if provided for free. *-Replacement feeding* is already used. Barriers to replacement feeding are high cost and requirement for cleanliness and health education. *-Formula feeding* was considered impractical (except for people living in urban settings with salaries). *-EBF* is not common practice due to the belief that EBF is not enough. *-Heat-treating breast milk* was considered impractical, except for some urban people	Findings from this study regarding *feasibility* and *acceptability* of heat treatment: Heat treatment was not seen as acceptable due to practical (feasibility) issues (complex and time consuming).

		with salaries, due to the fact that these options are complex and time consuming.	
Reference Israel-Ballard *et al.* (2006:48–60) Acceptability of heat treating breast milk to prevent mother-to-child transmission of human immunodeficiency virus in Zimbabwe: A qualitative study	**Focus of the study** To explore knowledge of, attitudes towards and resources required for heat-treating EBM as a potential infant-feeding option for HIV-positive mothers in Zimbabwe (FH and Holder methods)	**Bottom-line findings** *Current practice of expressing breast milk:* The practice of expressing breast milk was more common among working women. Rural-based participants had different experiences than urban participants. The major concern with expressing breast milk was the inability to bond with the child. However, after discussion, participants (from both urban and rural areas) believed that this could be overcome. *Cultural taboos (confession and contamination):* Although knowledge of cultural beliefs were consistent among both participants (rural and urban) and health workers, participants in urban and suburban areas had less attachment to such beliefs compared to participants in rural areas. However, after discussion, participants believed that these cultural taboos could be overcome. *Social stigma:* The community and the household expressed fears for rejection: Expressing of breast milk could indicate that mother is HIV positive. Participants agreed that inequalities between men and women limit safe breastfeeding practices. The man is usually the decision maker. When the woman decides on feeding options independently from her spouse, this could cause dissolved marriages. Through discussion views changed – participants discovered that heat treatment could be life saving. *Feasibility of expressing and heat-treating human milk: Resources and education:* Participants were interested to hear that heat treatment could kill the HI virus. However, they were sceptic that heat treatment could reduce the nutritional value of the EBM (request for evidence!). *Feasibility:* Greatest benefit of heat treatment was seen as the affordability, however, it was regarded as time consuming. Heat treatment was regarded more feasible throughout the discussion. *Equipment and education:* Participants preferred FH above the Holder method after demonstration due to the minimal equipment required. Participants agreed that health education is the most important resource.	**Findings relevant to this study** Findings from this study regarding *feasibility* and *acceptability* of FH: FH was seen as more feasible after discussion and demonstration. Affordability was seen as the greatest benefit. FH was seen as more acceptable throughout the discussion (views changed). Cultural taboos and stigma could be overcome. Health education was considered as the most important resource. Note: This study is one of the few studies that addresses *feasibility* and *acceptability* of particularly the FH method.

Reference	Focus of the study	Bottom-line findings	Findings relevant to this study
Leshabari *et al*. (2006:1–14) Translating global recommendations on HIV and infant feeding to the local context: The development of culturally sensitive counselling tools in the Kilimanjaro region: Tanzania	To describe the process used to develop a set of culturally sensitive, evidence-based counselling tools (job aids) to contribute to improving infant-feeding counselling services for HIV-positive women in the Kilimanjaro region of Tanzania	Participants strongly overestimated the relative risk of transmission during pregnancy, delivery and breastfeeding. Knowledge, practices and beliefs associated with HIV / infant-feeding options *EBF* was not seen as feasible beyond three months because breast milk was considered insufficient for the child's growth. *Cows' milk* was not generally regarded as an adequate replacement for breast milk unless the mother had died or had very good health reasons not to breastfeed. *Commercial infant formula* was not considered the best way to feed an infant due to the cost and uncertainly of how to use it. *Expression and heat-treatment of breast milk* were seen as not feasible due to it being time consuming and due to cultural beliefs. According to some, nurse counsellor 'informants' providing health education on this technique is important. *Wet nursing* was not considered feasible because of a fear for stigma. *In general:* Not breastfeeding but using replacement feeding and EBF was perceived as unacceptable. Participants experienced social pressure and a lack of control. Therefore, most participants ended up breastfeeding (some after initiating replacement feeding). Furthermore, a lack of knowledge of and confidence in implementing the recommended feeding options was mentioned by the participants.	Findings from this study concerning *feasibility* and *acceptability* of heat treatment: Heat treatment was seen as not feasible (due to the view that it was too time consuming) and unacceptable (due to cultural beliefs). Health education is vital to increase the lack of knowledge (and feasibility and acceptability).
Reference	**Focus of the study**	**Bottom-line findings**	**Findings relevant to this study**
Pullen *et al*. (2002) Attitudes of HIV infected mothers towards expressed and pasteurized breast milk for infant feeding	To determine the attitudes of HIV-infected mothers towards expressing and pasteurising breast milk for own infant feeding	All the mothers (n = 10) that were interviewed indicated that they were positive towards the PP method. Five mothers requested assistance due to a lack of financial resources or facilities for safe alternative infant-feeding methods. Two mothers expressed fears concerning an inability to produce sufficient breast milk (n = 1) and the disclosure of HIV status (n = 1).	Findings from this study concerning the *feasibility* and *acceptability* of PP: Overall, the PP method was seen as a feasible and acceptable method.
Experimental studies (n=1)			
Reference	**Focus of the study**	**Bottom-line findings**	**Findings relevant to this study**
Jeffery & Mercer (2000:219–223) Pretoria pasteurization: A potential method for the reduction of postnatal mother to child transmission of the human immunodeficiency virus	To test the reliability (in terms of *safety*) of PP under a range of conditions	The process of PP was found reliable with a narrow 95% CI for each set of starting conditions tested. The milk temperature remained between 56 and 62.5 °C for 10 to 15 minutes. The ambient temperature had minimal effect on temperature curves obtained. Critical note: Inability to test as wide a range as desired due to warm summer weather during the study.	Findings from this study concerning the *safety* (reliability) of PP: PP was considered reliable (in terms of safety) under a range of conditions.

4.2.3 Analysis strategy

In this study, meta-analysis was not appropriate, as both qualitative and quantitative studies were included and more than one question was stated. Data could therefore not be combined and analysed. An alternative strategy was used by providing a summary of the relevant findings of each study.

Thematic analysis was used for the synthesis process. The method of thematic analysis is used to identify major or recurrent themes in studies, followed by a summary of the findings under these thematic headings (Dixon-Woods *et al.*, 2006:15).

After the findings regarding each theme were combined in a summary of findings, the conclusion statement was developed.

4.2.4 Summary of the findings

A conclusion of the summary of the findings regarding the included studies according to the following research question is provided:

How effective is heat treatment of EBM as an in-home procedure in terms of (1) eliminating/ inactivating the HI virus and safety in terms of retaining the protective and nutritional value of the EBM; (2) feasibility as an in-home procedure; and (3) acceptability by the mothers and their communities?

In order to answer this research question, a summary of findings is provided of the included studies (final sample) according to the categories *safety*, *feasibility* and *acceptability* and according to these categories in the specific settings (rural vs. urban).

4.2.4.1 Safety

The outcomes measured to determine safety were the following:

a) Eliminate/inactivate the HI virus

Both pasteurisation methods (flash-heating and Pretoria pasteurisation) are able to eliminate/inactivate the HI virus (both methods inactivate HIV-1 up to> 3 logs) (Israel-Ballard *et al.*, 2005: Grade I evidence; Israel-Ballard, 2007: Grade I evidence; Jeffery *et al.,* 2001: Grade II evidence).

b) Retain the protective and nutritional value of the EBM

Both methods of pasteurisation do not produce a significant decrease in vitamins (besides decreases in vitamin C and E that were noted) and protective elements (such as lactoferrin and lysozyme surviving digestion). Both methods eliminated spiked bacteria (*E.coli* and *s. aureus*), retained the nutritional value and destroyed bacterial contamination. However, flash-heating was superior to Pretoria pasteurisation in retaining more antibacterial activity (Israel-Ballard *et al*., 2005: Grade I evidence).

Flash-heating significantly decreased the concentrations of IgA and IgG, anti-HIV-1, anti-pneumococcal polysaccharide and anti-poliovirus. In contrast, it increased the binding capacity of IgA to influenza. Flash-heated milk retains most (66%) of the antibody specificity (IgA and IgG) for the microbial antigens tested, and therefore offers similar protection with unheated milk (Chantry, *et al*., 2009: Grade II evidence).

Flash-heating requires further research to confirm the stability of nutritional, immunological and anti-microbial value and safety in different settings (such as field settings instead of laboratory settings) (Chantry *et al.*, 2009: Grade II evidence; Israel-Ballard, 2007: Grade I evidence).

Pretoria pasteurisation is found reliable under a range of conditions (such as different volumes of milk and the initial and ambient temperature of milk), but needs refined research. After refined research Pretoria pasteurization might be safe in retaining benefits such as the nutritional and anti-microbial value of breastfeeding (Jeffery & Mercer, 2000: Grade II evidence).

Conclusion statement 1

Both pasteurisation methods (flash-heating and Pretoria pasteurisation) are safe in terms of *eliminating/inactivating the HI virus*. In terms of *retaining the protective and nutritional value of the EBM*, none of the methods of pasteurisation significantly decreased protective factors such as lactoferrin and lysozyme surviving digestion or the nutritional value (such as vitamins) of the breast milk. Both methods might be safe for women in developing and developed settings, but require further testing.

4.2.4.2 Feasibility

Heat treatment of EBM is feasible in the weaning period after six months (up to 24 months), when milk is well established or partially used in times of increased risk of HIV transmission

(e.g. mastitis) (Coutsoudis, 2005: Grade II evidence; Israel-Ballard *et al*., 2006 & Israel-Ballard, 2007: Grade I evidence).

Heat treatment is affordable (both flash-heating and Pretoria pasteurisation) (Israel-Ballard *et al*., 2006: Grade I evidence). However, disadvantages were mentioned, such as heat treatment was seen as too time consuming and it requires skill and proper facilities (e.g. a heat source and fuel) (De Paoli *et al.*, 2003: Grade IV evidence; Israel-Ballard *et al.*, 2006: Grade I evidence).

Both methods require further testing regarding feasibility. The flash-heating method requires further testing of feasibility in general (Israel-Ballard *et al.*, 2005: Grade I evidence) and the Pretoria pasteurisation method requires investigation of feasibility as an in-home treatment (after discharge from hospital and in healthy, full-term infants) (Pullen *et al.*, 2003: Grade I evidence).

Conclusion statement 2

Regarding the feasibility of heat treatment of HIV-positive EBM:

2a) Heat-treatment methods could be affordable although it may be too time consuming.

2b) Heat treatment (flash-heating and Pretoria pasteurisation) can only be feasible if the user is skilled and the proper facilities available

2c) Further research is needed to confirm feasibility under a variety of conditions.

4.2.4.3 Acceptability

Heat treatment of EBM is not well accepted (Burke, 2004: Grade III evidence; Coutsoudis, 2004: Grade II evidence; De Paoli *et al*., 2003: Grade IV evidence; Leshabari *et al*., 2006: Grade IV evidence). The level of acceptability in rural areas compared to urban areas differed. In (sub)urban areas there is more acceptability of heat treatment of EBM (Israel-Ballard *et al.*, 2006: Grade I evidence). Researchers agreed that acceptability in rural areas was less than in urban areas (De Paoli *et al.*, 2003: Grade IV evidence; Israel-Ballard *et al.*, 2006 and Pullen *et al*., 2002: Grade I evidence). People in rural areas expressed less confidence due to a fear of stigma (suspicion of neighbours and family concerning the HIV status of the mother using heat treatment as an infant-feeding method) (De Paoli *et al.*, 2003: Grade IV evidence; Pullen *et al*., 2002: Grade I evidence). Contrary to people in rural areas, people in urban areas are more able to receive education and follow advice (Burke, 2004: Grade III evidence).

Acceptability is strongly influenced by cultural taboos (especially in rural areas) (Israel-Ballard *et al.*, 2006: Grade I evidence) and fear of stigma (family, neighbours and the community could be suspicious regarding HIV) (Burke, 2004: Grade III evidence; Coutsoudis, 2004: Grade II evidence; De Paoli, 2003: Grade IV evidence; Pullen *et al.*, 2002: Grade I evidence).

Acceptability of flash-heating increased after health education (Israel-Ballard *et al.*, 2006: Grade I evidence). Counselling and demonstration of heat treatment are important to reduce stigma and increase acceptability (Burke, 2004: Grade III evidence; Israel-Ballard *et al.*, 2006: Grade I evidence).

In general, more research is required on the acceptability of heat treatment of EBM in a variety of settings, especially in rural areas, where the implementation of safe infant-feeding options such as heat treatment faces difficulties (De Paoli *et al*., 2003: Grade IV evidence), and on the supporting of mothers in their choice of the method of infant feeding (Israel-Ballard *et al.,* 2005: Grade I evidence).

Conclusion statement 3

3a) Heat treatment of EBM is not well accepted, especially in rural areas due to a fear of stigma (suspicion of neighbours and family concerning the HIV status of the mother using heat treatment as an infant-feeding method) and cultural taboos.

3b) Acceptability of flash-heating can be improved through health education, counselling and practical demonstrations of heat-treatment methods.

3c) More research is required on the acceptability of heat treatment of EBM in a variety of settings, especially in rural areas, where the implementation of safe infant-feeding options such as heat treatment faces difficulties.

3d) Against the background of stigma associated with HIV and AIDS, more research is needed on the supporting of mothers in their choice of infant-feeding method.

4.2.4.4 Statements regarding the evidence

These statements include the overall summary statement (the level of agreement between studies), the comparison factor statement (important comparison factors), methodological

statements (types of research design used), outcome impact statements (existence of interventions/intervening factors that affected the outcomes) and definitions (key terms/definitions used in the judgement of usefulness) (ADA, 2008:56–57).

Conclusion statement 4

Methodological statements:

In general, it can be stated that the studies conducted with good/strong-medium evidence were five RCTs concerning the safety of both methods (Chantry *et al.*, 2009; Israel-Ballard, 2007; Israel-Ballard *et al.*, 2005; Jeffery *et al.*, 2001; Jeffery *et al.,* 2003) and two qualitative studies on the feasibility and acceptability (Israel-Ballard *et al.*, 2006; Pullen *et al.*, 2002) of the methods. The study that was graded as one of the lowest (poor/limited evidence) was a qualitative study on the *feasibility* and *acceptability* of heat treatment in general (Burke, 2004). For a detailed discussion, see Table 3.6 and paragraph 4.2.1.

Conclusion statement 5

Operationalisation of the core variable of heat treatment:

Heat treatment was inconsistently operationalised in the studies. One study (not included in the critical appraisal) mentioned 'boiling' of the breast milk (Hartmann *et al.*, 2006), while most of the others mentioned 'pasteurisation' (Chantry *et al.*, 2009; Jeffery *et al.,* 2001; Jeffery *et al.*, 2003; Jeffery & Mercer, 2000) or 'heat treatment' (Burke, 2004; Coutsoudis, 2005; De Paoli, 2003; Israel-Ballard *et al.*, 2005; Israel-Ballard *et al.*, 2006; Israel-Ballard, 2007; Leshabari *et al.*, 2006). Most of the studies that used 'pasteurisation' were studies concerning Pretoria pasteurisation, while most of the studies that used 'heat treatment' were studies concerning flash-heating.

4.3 SUMMARY

In this chapter, the realisation of the data extraction and data synthesis according to the steps of a systematic review were explained and characteristics of the final sample were provided. In order to answer the research question, a summary of findings was provided of the reviewed studies (the final sample) according to the categories *safety*, *feasibility* and *acceptability* and according to these categories in the specific settings (rural vs. urban). Conclusion statements were provided.

CHAPTER 5:

CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS

5.1 INTRODUCTION

An overview of the conclusion statement of the findings regarding each issue (e.g. *safety*, *feasibility* and *acceptability*), the evaluation of rigour and a discussion of limitations are provided in this chapter. Recommendations for research, education and nursing practice are also provided.

5.2 CONCLUSIONS

The following question was stated in Chapter 1: *How effective is heat treatment of EBM as an in-home procedure in terms of (1) eliminating/ inactivating the HI virus and safety in terms of retaining the protective and nutritional value of the EBM; (2) feasibility as an in-home procedure; and (3) acceptability by the mothers and their communities?*

To answer the question, conclusion statements have been developed, which are outlined as follows:

Conclusion statement 1

Both pasteurisation methods (flash-heating and Pretoria pasteurisation) are capable of eliminating/inactivating the HI virus and are therefore safe in terms of *eliminating/inactivating the HI virus*. In terms of *retaining the protective and nutritional value of the EBM*, none of the methods of pasteurisation significantly decreased protective factors such as lactoferrin and lysozyme surviving digestion or the nutritional value (such as vitamins) of the breast milk. Both methods might be safe for both women in developing and developed settings, but require further testing.

Conclusion statement 2

Regarding the feasibility of heat treatment of HIV-positive EBM:

2a) Heat-treatment methods could be affordable although it may be too time consuming.

2b) Heat treatment (flash-heating and Pretoria pasteurisation) can only be feasible if the user is skilled and has the proper facilities available.

2c) Further research is needed to confirm feasibility under a variety of conditions.

Conclusion statement 3

3a) Heat treatment of EBM is not well accepted, especially in rural areas due to a fear of stigma (suspicion of neighbours and family concerning the HIV status of the mother using heat treatment as an infant-feeding method) and cultural taboos.

3b) Acceptability of flash-heating can be improved through health education, counselling and practical demonstrations of heat-treatment methods.

3c) More research is required on the acceptability of heat treatment of EBM in a variety of settings, especially in rural areas, where the implementation of safe infant-feeding options such as heat treatment faces difficulties.

3d) Against the background of stigma associated with HIV and AIDS, more research is needed on the supporting of mothers in their choice of infant-feeding method.

Conclusion statement 4

Methodological statements:

Most of the studies included in this review are of good/strong-medium evidence.

Conclusion statement 5

Operationalisation of the core variable of heat treatment:

Heat treatment was inconsistently operationalised in the studies.

Bottom-line answer:

Heat treatment of EBM should be emphasised as a safe alternative for feeding exposed infants (those of an HIV-positive mother, those of uncertain HIV status or during weaning if the mother cannot afford formula or cow's milk), but should be supported with appropriate information to the individual mother, her family and the community.

5.3 EVALUATION OF RIGOUR

To increase rigour in all types of reviews (particularly systematic reviews and meta-analyses), all research decisions must be motivated in the different stages of the review, namely the problem-identification stage, the literature search stage, the critical appraisal stage, the data synthesis stage and the presentation (Whittemore & Knafl, 2005:548–552).

5.3.1 Problem-identification stage

In this systematic review, the problem and purpose were clearly stated and supported by evidence of a preliminary literature review. The review question was developed using the PICOTS format (see Table 3.1). Terminology/concepts used in the review were

systematically defined (see Table 1.1) (Bravata *et al.,* 2005:1063). Furthermore, both a conceptual model (Botes's model for nursing research) and a theoretical framework (model for evidence-based clinical decisions [Haynes *et al.*, 2002]) were used, which provided both a basis and support for the problem stated (Bravata *et al.*, 2005:1063). A systematic review was chosen as a design to answer the review question stated (see paragraph 1.7). Because of the rigorous methods used in systematic review to summarise the best information, conclusions derived from the systematic review are evidence that can be considered as high-quality evidence. This evidence can be used to inform practice and help in the making of clinical decisions (regarding safe infant-feeding options) that are based on high-quality evidence.

5.3.2 Literature search stage

The literature search was clearly described (O'Mathuna *et al*., 2008:104) and conducted as thoroughly as possible by identification of a complete and unbiased set of relevant studies to increase *internal validity* (Badr, 2007:80; Hopewell *et al.,* 2008:3). Therefore, the literature search strategy (sampling) was conducted as broadly and comprehensively as possible, including a broad combination of keywords, a variety of sources and clearly stated inclusion and exclusion criteria to ensure that no data that are relevant to the review topic were missed. To reduce *publication bias* (positive results that receive priority within publications compared to negative results), grey literature, such as conference papers, was scanned (Kitchenham, 2004:8). To reduce *language bias*, which refers to the possibility that studies are published in English only (O'Mathuna *et al.,* 2008:105), Afrikaans, English and Dutch studies were included if appropriate. An experienced librarian at the Ferdinand Postma Library at North-West University in Potchefstroom assisted with the literature search. In addition, authors were contacted when studies were not available (Badr, 2007:80).

5.3.3 Critical appraisal stage

Critical appraisal was conducted to ensure that only high-quality evidence was included for data extraction. In the critical appraisal phase, the researcher focussed on the appropriateness of the study design of the included studies in relation to the research question rather than focussing on the type of design. 'High-quality' types of research designs can be conducted in an inappropriate and biased way (CRD, 2009:33).

The following tools were used to appraise the relevant study designs:

- Critical appraisal instrument for reviews, RCTs, cohort studies and qualitative research (CASP, 2006)
- The evaluation tool for quantitative research studies (HCPRDU, 2005)

- The critical appraisal guidelines for single case study research (Atkins & Sampson, 2002:107)
- The JHNEBP research evidence appraisal tool (Newhouse *et al.,* 2007:206)

The tools were chosen based on their ability to fit the design of the included studies best. To prevent inconsistency, which could be caused due to a lack of the reviewer's skills to critically asses and interpret the designs/studies (CRD, 2009:34; Scott *et al.,* 2007:685) and to ensure that only studies that contain high-quality evidence would be included, the critical appraisal process was conducted by both the reviewer and an independent reviewer under supervision of experienced researchers, as they were familiar with the conducting of systematic reviews (see paragraph 3.4). To ensure transparency and repeatability, the entire search strategy was documented (including decisions concerning including/excluding data and reasons), which is presented in tables and a flowchart (see figures 3.1 and 3.2 and tables 3.4 to 3.6). The researcher took auditability into consideration (see paragraph 1.9) by establishing decision rules (such as the inclusion and exclusion criteria) for categorising data. As a final step to increase *internal validity* to ensure that no relevant data were missed, the search was updated before final submission of the research report (see paragraph 3.2).

5.3.4 Data synthesis stage

An overview of the data analysis process is provided in the text (see paragraph 4.2.3). Items to be included were carefully considered. To provide rigorous conclusions and recommendations, they were only derived from the evidence (Badr, 2007:80).

5.3.5 Presentation

A separate chapter reports on the conclusions, recommendations and limitations of the study. Furthermore, the outcomes of the systematic review will be submitted for publication in a peer-reviewed journal. The entire systematic review was presented as transparently as possible using tables and flowcharts, where applicable. In addition, reporting was done as appropriately and detailed as possible to prevent missing any relevant information (CRD, 2009:41).

5.4 LIMITATIONS

The following limitations were identified:

- Only the electronically databases subscribed to by North-West University were used. This is a limitation (as for instance other universities might have more/different databases) as relevant data may have been missed. However, this was overcome by

using multiple sources to obtain both published studies, such as electronic databases, papers and catalogues, and unpublished studies (grey literature). A manual search and contacting the authors ensured that no relevant data was missed.

- Although the search strategy was conducted as broadly and rigorously as possible, using different sources (see paragraph 3.2), it was not always possible to obtain abstracts (or hard copies (where applicable) of the articles. However, those studies that could not be obtained (including reasons) were recorded, and outlined in Table 3.4.
- In this study, blinding was not used during the search or critical appraisal steps, as there was no conflict of interest. This could be a limitation with regard to validity of appraisal. However, the critical appraisal was conducted by master's students who did not know the experts involved in the field.
- The researcher could not find evidence of the validity of the JHNEBP research evidence appraisal tool (Newhouse *et al.,* 2007:206) that was used. However, this tool met the criterion that it should fit the research design of the specific study (see paragraph 2.3.3) by its virtue that it can be used for both quantitative (experimental, quasi-experimental and non-experimental) and qualitative designs (see paragraph 3.4).

5.5 RECOMMENDATIONS

One of the attributes of a systematic review is that it can help to provide recommendations for future research, education and nursing practice. Based on the conclusion statements derived from the findings of the systematic review, the following recommendations for further research, education and nursing practice can be made. The recommendations provided are connected to the levels of evidence (see paragraph 2.3.3), as high-quality evidence will strengthen the recommendations (Oxman, 1994:649).

Recommendations for further research

- More experimental trials (preferably RCTs using a rigorous strategy that fits the research question) should be conducted, as there is insufficient evidence of the *nutritional* (retaining the protective value) and *antibacterial safety* of EBM of both methods under a range of conditions (Israel-Ballard, 2007 & Israel-Ballard *et al.,* 2005: Grade I evidence).
- Further field testing (by means of RCTs) is required with regard to the determination of the *feasibility* of heat treatment. Specifically, investigation regardless of the extent to which mothers in rural areas are able to express and heat treat their breast milk at home is necessary, since it was found that barriers to *feasibility* of heat treatment could be the

requirement of skills and proper facilities (such as heat source and fuel) (De Paoli *et al.*, 2003: Grade IV evidence; Israel-Ballard *et al.,* 2006: Grade I evidence).

- The role of stigma in acceptability needs to be investigated more by means of qualitative research, as it seems that *acceptability* of pasteurisation in general is limited by mainly the fear of stigma (Coutsoudis, 2005: Grade II evidence; De Paoli *et al.,* 2003: Grade IV evidence; Pullen *et al.*, 2002: Grade I evidence). In addition, the acceptability of both methods should be investigated in general by means of studies using qualitative methods conducted in different settings (rural versus urban) (Israel-Ballard *et al*., 2005: Grade I evidence).
- Further research is needed on the supporting of HIV-positive mothers in their infant-feeding choice (Israel-Ballard *et al.,* 2005: Grade I evidence).

Recommendations for nursing education

- Curriculum content in basic training programmes of nurses and midwives should include evidence-based information on heat treatment to enable them to provide HIV-positive mothers with health education.
- Clinical practitioners should be trained to be able to counsel and demonstrate heat treatment to offer HIV-infected mothers evidence-based health education to empower them to make an informed choice regarding infant feeding and to limit MTCT of the HI virus.

Recommendations for nursing practice

It is recommended that clinical practitioners keep up to date with the best evidence of heat treatment (evidence in this systematic review could for example be used, because this study design strived to include all relevant studies) to improve their health education to enable HIV-positive mothers to make an informed decision regarding infant feeding and thereby limit MTCT of the HI virus. Although heat treatment was not well accepted mainly due to fear for stigma (Coutsoudis, 2005: Grade II evidence; De Paoli *et al.*, 2003: Grade IV evidence; Israel-Ballard *et al.,* 2005: Grade I evidence; Pullen *et al.*, 2002: Grade I evidence), it was found that perceptions of heat treatment can be changed positively by increased health education (Israel-Ballard *et al*., 2006: Grade I evidence). Improving health education could therefore play an important role in increasing acceptability.

Heat treatment of EBM as infant-feeding method should be recommended in the following situations: when the HIV-positive mother starts to work; in situations of breast health problems; when starting with solid foods (after six months); and when breast feeding is not

given exclusively anymore, but the mother cannot afford formula/cow's milk alternatives (Burke, 2004: Grade III evidence; Coutsoudis, 2005: Grade II evidence).

5.6 AIM

This study answered the research question. Existing evidence of the effectiveness in terms of *safety, feasibility* and *acceptability* of heat treatment of EBM, particularly the Pretoria pasteurisation method, used as an in-home procedure in urban and specifically rural settings, is insufficient and more research is needed.

5.7 SUMMARY

In this chapter, an overview of the conclusion statement of the findings regarding each issue (e.g. *safety*, *feasibility* and *acceptability*) was provided. The evaluation of rigour and a discussion of limitations were given. Finally, recommendations regarding research, education and nursing practice were provided and an explanation of whether the aim of the study was reached was given. In order to implement the research evidence gleaned from this systematic review, the evidence should be integrated with the clinical expertise of the health worker; the HIV-positive mother's preferences, values and actions; and the clinical state and circumstances of the HIV-positive mother, for it is the HIV-positive mother (and where appropriate, her family) who makes the final decisions regarding her baby's health.

REFERENCE LIST[1]

ABRAMS, B. 2007. HIV, exclusive breastfeeding and weaning in sub-Saharan Africa: Can flash-heating breast milk help bridge the gap? *Future HIV Therapy,* 1(3):235–238.

ADA see AMERICAN DIETETIC ASSOCIATION.

AKOBENG, A.K. 2005. Understanding systematic reviews and meta-analysis. *Archives of Disease in Childhood,* 90:845–848.

ALLAN, H., BADENOCH, D., BEXON, N., CARLSSON, C., DEARNESS, K., MIHAILOVA, B. & WEST, J. S.a. An introduction to evidence-based health care. In Critical Appraisal Skills Programme (CASP) as part of the Public Health Resource Unit. [CD].

ALTMAN, D.G. 1999. What randomized trials and systematic reviews can offer decision makers. *Hormone Research,* 51(Suppl. 1):36–43.

AMERICAN DIETETIC ASSOCIATION. 2008. *Evidence analysis manual: Steps in the ADA evidence analysis process*. Chicago: Scientific Affairs and Research, American Dietetic Association. 88p.

ATKINS, C. & SAMPSON, J. 2002. Critical appraisal guidelines for single case study research. *ECIS* Jun:100–109.

BADGETT, R.G., O'KEEFE, M. & HENDERSON, M.C. 1997. Using systematic reviews in clinical education. *Annals of Internal Medicine,* 126(11):886–891.

BADR, E. 2007. Making use of systematic reviews. *Sudanese Journal of Public Health,* 2:79–80.

[1] According to VAN DER WALT, E.J. 2006. *Quoting sources.* Potchefstroom: Ferdinand Postma Library, North-West University, Potchefstroom Campus. Available: http://www.nwu.ac.za/library/documents/verwysings.pdf Date of access: 20 February 2009.

BECK, C.T. 1993. Qualitative research: The evaluation of its credibility, fittingness and auditability. *Western Journal of Nursing Research,* 15(2):263–266.

BESA see BUSSINESS ETHICS SOUTH AFRICA.

BOTES, A.C. 1992. 'n Model vir kwalitatiewe navorsing in die verpleegkunde. *Curatonis,* 15(4):36–42.

BRAVATA, D.M., MCDONALD, K.M., SHOJANIA, K.G., SUNDARAM, V. & OWENS, D.K. 2005. Challenges in systematic reviews: Synthesis of topics related to the delivery, organization, and financing of health care. *Annals of Internal Medicine,* 142(12) part 2:1056–1065.

BRINK, H. 2006. *Fundamentals of research methodology for health care professionals*. Second edition. Cape Town: Juta. 226 p.

BURKE, J. 2004. Infant HIV infection: Acceptability of preventive strategies in central Tanzania. *AIDS Education and Prevention,* 16(5):415–425.

BURNS, N. & GROVE, S.K. 2005. *The practice of nursing research: Conduct, critique and utilization*. Fifth edition. St Louis: Elsevier Saunders. 780 p.

BUSINESS ETHICS SOUTH AFRICA. S.a. In North-West University (NWU). 2007. *Manual for postgraduate studies*. Potchefstroom: North-West University.

CASP see CRITICAL APPRAISAL SKILLS PROGRAMME.

CEBC see CENTRE FOR EVIDENCE-BASED CONSERVATION.

CENTRE FOR EVIDENCE-BASED CONSERVATION. 2009. *Guidelines for systematic review in conservation and environmental management* . Bangor, Gwyneth: Bangor University. http://www.cebc.bangor.ac.uk/Documents/Reviewguidelinesversion3.0_FINAL pdf Date of access: 14 May 2009.

CENTRE FOR REVIEWS AND DISSEMINATION. 2009. *Systematic reviews: CRD's guidance for undertaking reviews in health care*. York: University of York. 281p.

CHANTRY, C.J., ISRAEL-BALLARD, K., MOLDOVEANU, Z., PEERSON, J., COUTSOUDIS, A., SIBEKO, L. & ABRAMS, B. 2009. Effect of flash-heat treatment on immunoglobulins in breast milk. *Journal of Acquired Immune Deficiency Syndromes,* 51(3):264–267.

CLOSS, S.J. & CHEATER, F.M. 1999. Evidence for nursing practice: A clarification of the issues. *Journal of Advanced Nursing,* 30(1):10–17.

COOK, D.J., GREENGOLD, N.L., ELLRODT, A.G. & WEINGARTEN, S.R. 1997. The relation between systematic reviews and practice guidelines. *Annals of Internal Medicine,*127:210–216.

COOK, D.J., MULROW, C.D. & HAYNES, R.B. 1997. Systematic reviews: Synthesis of best evidence for clinical decisions. *Annals of Internal Medicine,* 26(5):376–380.

COUTSOUDIS, A. 2005. Infant feeding dilemmas created by HIV: South African experiences. *Journal of Nutrition,* 1315:956–959.

COUTSOUDIS, A., GOGA, A.E., ROLLINS, N. & COOVADIA, H.M., ON BEHALF OF THE CHILD HEALTH GROUP. 2002. Free formula milk for infants of HIV-infected women: Blessing or curse? *Health Policy Plan,* 17(2):154–160.

CRD see CENTRE FOR REVIEWS AND DISSEMINATION.

CRITICAL APPRAISAL SKILLS PROGRAMME. 2006. *Evidence-based health care*. Oxford: Public Health Resource Unit.
http://www.phru.nhs.uklcaspl critical ~appraisal ~tools.htm Date of access: 5 March 2009.

CROWTHER, M.A. & COOK, D.J. 2007. Trials and tribulations of systematic reviews and meta-analyses. *Hematology*, (1):493–497.

CUMMINGS, G. 2007. *Systematic reviews: Protocol for completing systematic reviews*. (Unpublished).

DE PAOLI , M.M., MANONGI, R. & KLEPP, K-I. 2003. Are infant feeding options that

are recommended for mothers with HIV acceptable, feasible, affordable, sustainable and safe? Pregnant women's perspectives. *Public Health Nutrition,* 7(5):611–619.

DIXON-WOODS, M., BONAS, S., BOOTH, A., JONES, D.A., MILLER, T., SUTTON, A.J., SHAW, R.L., SMITH, J.A. & YOUNG, B. 2006. How can systematic reviews incorporate qualitative research? A critical perspective. *Qualitative Research*, 6:27–44.

EGLIN, R.P. & WILKINSON, A.R. 1987. HIV infection and pasteurisation of breastmilk. *Lancet,* 1:1093.

ELLIS, M.V. 1991. Conducting and reporting integrative research reviews. *Counsellor, Education and Supervision,* 30(3):225–238.

EYSENBACH, G., TUISCHE, J. & DIEPGEN, T.L. 2001. Evaluation of the usefulness of internet searches to identify unpublished clinical trials for systematic reviews. *Medical Informatics & the Internet in Medicine,* 26(3):203–218.

EVANS, D. 2003. Hierarchy of evidence: A framework for ranking evidence evaluating healthcare interventions. *Journal of Clinical Nursing*, 12:77–84.

FLEMMING, K. 2007. The synthesis of qualitative research and evidence-based nursing. *Evidence- Based Nursing,* 10:68–71.

FORREST, J.L. & MILLER, S.A. 2004. Part I: The anatomy of evidenced-based publications: Article summaries and systematic reviews. *The Journal of Dental Hygiene,* 78(II):343–348.

FOX, D. 2005. Evidence of evidence-based health policy: The politics of systematic reviews in coverage decisions. *Health Affairs*, 24(1):14–122.

FRENCH, P. 1999. The development of evidence-based nursing. *Journal of Advanced Nursing,* 29(1):72–78.

FRYMARK, T., SCHOOLING, T., MULLEN, R., WHEELER-HEGLAND, K., ASHFORD, J., MCCABE, D., MUSSON, N. & HAMMOND, C.S. 2009. Evidence-based systematic review: Oropharyngeal dysphagia behavioural treatments. Part I: Background and methodology. *Journal of Rehabilitation Research & Development,* 46(2):175–184.

GEORGE, J.B. 1990. *Nursing theories: The base for professional nursing practice*. Third edition. New Jersey: Prentice-Hall International.

GILES, M. & MIJCH, A. 2005. Breastmilk pasteurization in developed countries to reduce HIV transmission: Do the benefits overweight the risks? *Infectious Diseases in Obstetrics and Gynecology*, 13(4):237–240. Dec.

GOLDBLUM, R.M., DILL, C.W., ALBRECHT, T.B., ALFORD, E.S., GARZA, C. & GOLDMAN, A.S. 1984. Rapid high-temperature treatment of human milk. *The Journal of Pediatrics,* 104(3):380–385.

GREENHALGH, T. 1997. How to read a paper: Getting your bearings (deciding what the paper is about). *British Medical Journal,* 315:243–246.

GREER, N., MOSSER, G., LOGAN, G. & WAGSTROM HALAAS, G. 2000. A practical approach to evidence grading. *Journal Quality Improvement,* 26:700–712. (*In* American Dietetic Association (ADA). Evidence analysis manual: Steps in the ADA evidence analysis process. 2008. Chicago: Scientific Affairs and Research, American Dietetic Association.)

GUPTA, N. 2005. Basic health needs of people. Paper delivered at the Conference on People's Health: Determinants, Current Challenges and Opportunities, 14–15 May. Cairo, Egypt: Ain Shams University. http://www.ahedegypt.org/Conference/Presentations/Peoples_action_to_make_the_public_health_system.pdf Date of access: 3 June 2009.

HAYNES, R.B., DEVEREAUX, P.J. & GUYATT, G.H. 2002. Clinical expertise in the era of evidence-based medicine and patient choice. *Vox Sanguinis,* 83(Suppl. 1):383–386.

HARTMANN, S.U., BERLIN, C.M. & HOWETT, M.K. 2006. Alternative modified infant-feeding practices to prevent postnatal transmission of Human Immunodeficiency Virus type 1 through breast milk: Past, present and future. *Journal of Human Lactation,* 22(1):75-88.

HCPRDU see HEALTH CARE PRACTICE RESEARCH AND DEVELOPMENT UNIT.

HEALTH CARE PRACTICE RESEARCH AND DEVELOPMENT UNIT (HCPRDU). 2005. *Evaluation tool for quantitative research studies*. Manchester: University of Salford. http://www.fhsc.salford.ac.uk/hcprdu/quantitative.htm Date of access: 13 April 2009.

HOPEWELL, S., CLARKE, M.J., LEFEBVRE, C. & SCHERER, R.W. 2008. Hand searching vs. electronic searching to identify reports of randomized trials (Review). *Cochrane Database of Systematic Reviews*, 4:1–39.

INGERSOLL, G.L. 2000. Evidence-based nursing: What it is and what it isn't. *Nursing Outlook,* 48:151–152.

ISRAEL-BALLARD, K.A. 2007. Demonstrating the safety of flash-heated breast milk: A potential infant feeding option for HIV-positive mothers in developing countries. PhD dissertation. Berkeley: University of California.

ISRAEL-BALLARD, K.A., ABRAMS, B.F., COUTSOUDIS, A., SIBEKO, L.N., CHERYK, L.A. & CHANTRY, C.J. 2008. Vitamin content of breast milk from HIV-1-nfected mothers before and after flash-heat treatment. *Journal of Acquired Immune Deficiency Syndrome,* 48(4):444–448. Aug.

ISRAEL-BALLARD, K.A., MATHERNOWSKAM, C., ABRAMS, B.F., MORRISON, P., CITIBURA, L., CHIPATO, T., CHIRENJE, Z.M., PADIAN, N.S. & CHANTRY, C.J. 2006. Acceptability of heat treating breast milk to prevent mother-to-child transmission of human immunodeficiency virus in Zimbabwe: A qualitative study. *Journal of Human Lactation,* 22(1):48–60.

ISRAEL-BALLARD, K.A, CHANTRY, C., DEWEY, K., LONNERDAL, B., SHEPPARD, H., DONOVAN, R., CARLSON, J., SAGE, A. & ADAMS, B. 2005. Viral, nutritional and bacterial safety of flash-heated and Pretoria-pasteurized breastmilk to prevent mother-to-child transmission of HIV in resource-poor countries: A pilot study. *Journal of Acquired Immune Deficiency Syndrome,* 40(2):175–181. Oct.

ISRAEL-BALLARD, K.A., DONOVAN, R., CHANTRY, C.J., COUTSOUDIS, A., SHEPPARD, H., SIBEKO, L. & ABRAMS, A. 2007. Flash-heat inactivation of HIV-1 in human milk: A potential method to reduce postnatal transmission in developing countries. *Journal of Acquired Immune Deficiency Syndrome,* 45(3):318–323.

JBIEBNM see THE JOHANNA BRIGGS INSTITUTE FOR EVIDENCE BASED NURSING AND MIDWIFERY.

JEFFERY, B.S. & MERCER, K.G. 2000. Pretoria pasteurization: A potential method for the reduction of postnatal mother to child transmission of the human immunodeficiency virus. *Journal of Tropical Pediatrics,* 46:219–223. Aug.

JEFFERY, B.S., SOMA-PILLAY, P. & MOOLMAN, G. 2003. The effect of Pretoria pasteurization on bacterial contamination of hand-expressed human breastmilk. *Journal of Tropical Pediatrics,* 49:240–244.

JEFFERY, B.S., WEBBER, L., MOKHONDO, K.R. & ERASMUS, D. 2001. Determination of the effectiveness of inactivation of human immunodeficiency virus by Pretoria pasteurisation. *Journal of Tropical Pediatrics,* 47:345–349. Dec.

JOINT COMMITTEE ON HEALTH EDUCATION TERMINOLOGY. 1973. New definitions: Report of 1972–1973. *Health Education Monograph,* 33:63–70.

KATRAK, P., BIALOCERKOWSKI, A.E., MASSY-WESTROPP, N., KUMAR, V.S.S. & GRIMMER, K.A. 2004. A systematic review of the content of critical appraisal tools. *BioMed Central Medical Research Methodology,* 4(22):1–11.

KEELEY, P.W. 2004. Clinical guidelines. *Palliative Medicine*, 17:368–374.

KITCHENHAM, B. 2004. Procedures for performing systematic review. Keele: Software engineering group & Eversleigh: Empirical Software Engineering. July. http://www.idi.ntnu.no/emnee/empsc/papers/kitchenham_2004.pdf Date of access: 19 January 2009.

LAM, R.M. & KENNEDY, S.H. 2005. Using meta-analysis to evaluate evidence: Practical tips and traps. *Canadian Journal of Psychiatry,* 50(3):167–174.

LANDMAN, W.A., PUNT, W. & PAINTER-MORLAND, M. 2002. EthicSA Research Report No. 3. Business Ethics South Africa Survey 2002. In North-West University (NWU). 2007. *Manual for postgraduate studies*. Potchefstroom: North-West University.

LAUPACIS, A. & STRAUS, S. 2007. Systematic reviews: Time to address clinical and policy relevance as well as methodological rigor. *Annals of Internal Medicine,* 147:273–274.

LAWRENCE, R. & LAWRENCE, R. 2005. *Breastfeeding: A guide for the medical profession*. Sixth edition. St. Louis: Mosby. 1184 p.

LESHABARI, S.C., KONIZ-BOOHER, P., ASTROM, A.N., DE PAOLI, M.M. & MOLAND, K.M. 2006. Translating global recommendations on HIV and infant feeding to the local context: The development of culturally sensitive counselling tools in the Kilimanjaro region: Tanzania. *Implementation Sciences,* 1(22):1–14.

LEVY, M. 2009. The impact of consumers' health literacy on public health. *The Journal of Consumers Affairs*, 43(2):367–372.

LOBIONDO-WOOD, G. & HABER, J. 2002. Nursing research: Methods, critical appraisal and utilization. Fifth edition. St.Louis: Mosby. 520 p.

LUNDH, A. & GOTZSCHE P.C. 2008. Recommendations by Cochrane review groups for assessment of the risk of bias in studies. *BMC Medical Research Methodology,* 8(22):1–9.

MAGAREY, J.M. 2001. Elements of a systematic review. *International Journal of Nursing Practice,* 7:376–382.

MCDOUGAL, J.S., MARTIN, L.S., CORT, S.P., MOZEN, M., HELDEBRANT, C.M. & EVATT, B.L. 1985. Thermal inactivation of the acquired immunodeficiency syndrome virus T lypphotropic virus-III / lyphadenopathy-associated virus, with special reference to anti-themophilic factor. *Journal of Clinical Investigation,* 76:875–877. Aug.

MCGOWAN, J. & SAMPSON, M. 2005. Systematic reviews need systematic searchers. *Journal of Medical Library Association,* 93(1):74–80. Jan.

MCINTOSH, H.M., WOOLACOTT, N.F. & BAGNALL, A. 2004. Assessing harmful effects in systematic reviews. *BMC Medical Research Methodology*, 4(19):1–6.

MCKAY, J. & MARSHALL, P. 2000. Quality and rigour of action research in information systems. *Eighth European Conference on Information Systems.* Vienna: Edith Cowan University:1-11.

MCKIBBON, K.A. & MARKS, S. 1998a. Searching for the best evidence. Part 1: Where to look. *Evidence-based Nursing*, 1(3):68–70. Jul.

MCKIBBON, K.A. & MARKS, S. 1998b. Searching for the best evidence. Part 2: Searching CINAHL and Medline. *Evidence-based Nursing*, 1(4):105–107. Oct.

MELNYK, B.M. 2004. Integrating levels of evidence into clinical decision making. *Pediatric Nursing*, 30(4):323–325.

MELNYK, B.M. & FINEOUT-OVERHOLT, E. 2005. *Evidence-based practice in nursing and healthcare: A guide to best practice*. Philadelphia: Lippincott Williams & Wilkins. 608 p.

MINNIE, C.S. 2007. Best practice guidelines for counselling for HIV testing during pregnancy. PhD-thesis, Potchefstroom, North-West University. 292 p.

MORTAZ HEIJR, S. 2005. Critical Appraisal tools for systematic reviews. Systematic Review Study Group. http://ssrc.tums.ac.ir/SystematicReview/Appraisal-Tools.asp Date of access: 25 August 2009.

MOUTON, J. & MARAIS, H.C. 1994. *Basic concepts in the methodology of the social sciences*. Pretoria: Human Sciences Research Council. 269 p.

MULHALL, A. 1998. Nursing, research, and the evidence. *Evidence-based Nursing*,1:4–6. Jan.

NATIONAL DEPARTMENT OF HEALTH. 2008. *Policy and guidelines for the implementation of the PMTCT programme.*
http://www.doh.gov.za/docs/policy/pmtct.pdf Date of access: 15 October 2009.

NDoH see NATIONAL DEPARTMENT OF HEALTH.

NEWHOUSE, R.P., DEARHOLT, S.L., POE, S.S., PUGH, L.C. & WHITHE, K.M. 2007. *John Hopkins nursing evidence-based practice: Model and guidelines*. Indianapolis: Sigma Theta Tau International. 227 p.

NICOLL, A., NEWELL, M.L., PECKHAM, C., LUO, C. & SAVAGE, F. 2000. Infant feeding and HIV infection. *AIDS,* 14(Suppl. 3):S57–S74.

NIND, M. 2006. Conducting systematic review in education: A reflexive narrative. *London Review of Education*, 4(2):183–195. Jul.

OED see OXFORD ENGLISH DICTIONARY.

OERMANN, M.H., ROOP, J.C., NORDSTROM, C.K., GALVIN, E.A. & FLOYD, J.A. 2009. Effectiveness of an intervention for dissemination Cochrane reviews to nurses. *Urologic Nursing,* 29(1):35–54.

OLIVIER, P. 2003. *The students' guide to research ethics*. First edition. Maidenhead, Philadelphia: Open University Press. 156 p.

O'MATHUNA, D.P., FINEOUT-OVERHOLT, E. & KENT, B. 2008. How systematic reviews can foster evidence-based clinical decisions: Part II. *Worldviews on Evidence-based Nursing,* second quarter:102–107.

OXFORD ENGLISH DICTIONARY (OED) [Online]. 2009. Oxford: Oxford University Press. http//:www.askoxford.com Date of access: 5 March 2009.

OXMAN, A.D. 1994. Education and debate: Systematic reviews – checklists for review articles. *British Medical Journal,* 309:648–651. Sep. http://www.bmj.com/cgi/content/full/309/6955/648 Date of access: 15 September 2009.

PEARSON, A. 2005. A broader view of evidence. *International Journal of Nursing Practice,* 11:93–94.

PHRU see PUBLIC HEALTH RESOURCE UNIT.

POMERLEAU, J. 2001. *Development of a global strategy on infant and young child*

Feeding Report on a WHO/UNICEF consultation for the WHO European region. Budapest, Hungary, 28 May–1 June. WHO, Copenhagen. 104p.

POMPEO, D.A., ROSSI, L.A. & GALVAO, C.M. 2009. Integrative literature review: The initial step in the validation process of nursing diagnoses. *Acta Paul Enferm,* 22(4):434–438.

PUBLIC HEALTH RESOURCE UNIT.2007.FAQ's. http://www.phru.nhs.uk/Pages/PHD/FAQs.htm Date of access 4 November 2009.

PULLEN, A.E., MOKHONDO, K.R. & JEFFERY, B.S. 2002. Attitudes of HIV-infected mothers towards expressed and pasteurized breast milk for infant feeding. *MCR Unit for Maternal and Infant Healthcare Strategies.* Aug. http://www.qaproject.org/strat/Africa/South%20Africa/UNICEFAttitudes.pdf. Date of access: 20 February 2009.

RCN see ROYAL COLLEGE OF NURSING.

REGEHR, G. & BORDAGE, G. 2006. To blind or not to blind? What authors and reviewers prefer. *Medical Education,* 40:832–839.

ROSS, J.S., GROSS, C.P., DESAI, M.M., HONG, Y., GRANT, A.O., DANIELS, S.R., HACHINSKI, V.C., GIBBONS, R.J., GARDNER, T.J. & KRUMHOLZ, H.M. 2006. Effect of blinded peer review on abstract acceptance. *Journal of American Medical Association,* 295(14):1675–1680.

ROSSOUW, D. 2005. *Intellectual tools: Skills for the human sciences. Fundamentals of research methodology for health care professionals.* Pretoria: Van Schaik.

ROYAL COLLEGE OF NURSING (RCN). 2003. RCN nursing definition launched. *British Journal of Nursing*, 12(9):527.

RUF, A.J., COBERLY, J., HALSEY, N.A., BOULOS, R., DESORMEAUX, J., BURNLEY, A., JOSEPH, D.J., MCBRIEN, M., QUINN, T., LOSIKOFF, P., O'BRIEN, K.L., LOUIS, M.A. & FARZADEGAN, H. 1994. Prevalence of HIV-1 DNA and p24 antigen in breast milk and correlation with maternal factors. *Journal of Acquired Immune Deficiency Syndromes,* 7:68–73.

SACKETT, D.L., ROSENBERG, W.M.C., GRAY, J.A., HAYNES, R.B. & RICHARDSON, W.S. 1996. Evidence-based medicine: What it is and what it isn't. *British Medical Journal,* 312:71–72.

SACKETT, D.L., STRAUS, S., RICHARDSON, S.R., ROSENBERG, W. & HAYNES, R.B. 2000. *Evidence-based medicine: How to practice and teach EBM*. Second edition. London: Churchill Livingstone. 261p.

SCHOLTEN, R.J.P.M., CLARKE, M. & HETHERINGTON, J. 2005. The Cochrane collaboration. *European Journal of Clinical Nutrition*, 59(Suppl. 1):S147–S149.

SCOTT, N.A., MOGA, C., BARTON, P., RASHIQ, S., SCHOPFLOCHER, D. TAENZER, P. & HARSTALL, C. 2007. Creating clinically relevant knowledge from systematic reviews: The challenges of knowledge translation. *Journal of Evaluation in Clinical Practice,* 13:681–688.

SHEA, B., BOERS, M., GRIMSHAW, J.M., HAMEL, C. & BOUTER, L.M. 2006. Does updating improve the methodological and reporting quality of systematic reviews? *BioMedical central Research Methodology*, 6(27). http://www.biomedcentral.com/1471-2288/6/27 Date of access: 18 June 2009.

SUTHERLAND, S.E. 2004. An introduction to systematic reviews. *Journal of Evidence-based Dental Practice*, 4:47–51. Mar.

THE JOHANNA BRIGGS INSTITUTE FOR EVIDENCE BASED NURSING AND MIDWIFERY (JBIEBNM). 2000. *Appraising systematic reviews: Changing practice*. Suppl. 1: Evidence based practice information sheets for health professionals. http://www.joannabriggs.edu.au/CP1.pdf Date of access: 12 June 2009.

THIOR, I., LOCKMAN, S., SMEATON, L.M., SHAPIRO, R.L., WESTER, C., HEYMANN, S.J., GILBERT, P.B., STEVENS, L., PETER, T., KIM, S.Y., VAN WIDENFELT, E., MOFFAT, C., NDASE, P., ARIMI, P., KEBAABETSWE, P., MAZONDE, P., MAKHEMA, J., MCINTOSH, K., NOVITSKY, V., LEE, T.H., MARLINK, R., LAGAKOS, S. & ESSEX, M., FOR THE MASHI STUDY TEAM. 2006. Breastfeeding plus infant zidovudine prophylaxis for

6 months vs. formula feeding plus infant zidovudine for 1 month to reduce mother-to-child HIV transmission in Botswana: A randomized trial – the Mashi Study. *Journal of the American Medical Association,* 296(7):794–805.

THIRY, L., SPRECHER-GOLDBERGER, S., JONCKHEER, T., LEVY, J., VAN DE PERRE, P., HENRIVAUX, P., COGNIAUX-LECLERC, J. & CLUMECK, N. 1985. Isolation of Aids virus from cell-free breast milk of three healthy virus carriers. *Lancet,* 19(2):891–892. Oct.

VAN ZOEREN-GROBBEN, D., SCHRIJVER, J., VAN DEN BERG, H. & BERGER, H.M. 1987. Human milk vitamin after pasteurization, storage or tube feeding. *Archives of Diseases Childhood,* 62:161–165.

WELSH, J.K. & MAY, J.T. 1979. Anti-infective properties of breast milk. *Journal of Pediatrics,* 94:1-9.

WHEELER, D. 2000. The precise endeavour. Unpublished thesis, New Zealand: Massey University. (*In* C. Atkins & J. Sampson. Critical appraisal guidelines for single case study research. *ECIS*, June 2002:100–109.)

WHITTEMORE, R. & KNAFL, K. 2005. The integrative review: Updated methodology. *Journal of Advanced Nursing,* 52(5):546–553.

WHO see WORLD HEALTH ORGANIZATION.

WHO, UNAIDS, UNICEF & UNFPA. 2008. *HIV transmission through breastfeeding: A review of available evidence. An update from 2001–2007*. Geneva: WHO. http://whqlibdoc.who.int/publications/2008/9789241596596_eng.pdf Date of access: 26 January 2009.

WHO & UNICEF. 2008. *HIV and infant feeding counselling tools: Orientation guide for trainers*. Geneva: WHO. http://whqlibdoc.who.int/publications/2008/9789241596534_eng.pdf Date of access: 22 August 2009.

WORLD HEALTH ORGANIZATION (WHO). 2001. *Definitions and indicators in*

family planning, maternal & child health and reproductive health used in the WHO regional office for Europe. Geneva: WHO, Reproductive, Maternal and Child Health European Regional Office. 15p.

YEO, E.A., BEQUET, L., EKOUEVI D, K. & KRAWINKEL, M. 2002. Attitudes towards exclusive breastfeeding and other infant feeding options: A study from Abidjan, Côte d'Ivoire. *Journal of Tropical Pediatrics,* 51(4):223-226. Aug.

APPENDICES

Appendix 1.1

Table 1.1 Electronic databases and combination of keywords

Electronic databases	*Combination of keywords*	*Reasons*
ScienceDirect	(HIV or AIDS) **and** (heat or pasteuri* or steri* or boil*) **and** (milk or breast milk or human milk or mother* milk or feeding)	Full combination of keywords could be used. 235 results yielded.
EBSCOhost	(HIV or AIDS) **and** (heat or pasteuri* or steri* or boil*) **and** (milk or breast milk or human milk or mother* milk or feeding)	Full combination of keywords could be used. 155 results yielded.
Sabinet	(HIV or AIDS) **and** (milk or breast* or feeding or mother*) **and** (heat or pasteuri* or steri* or boil*)	Full combination of keywords could be used. 92 results yielded.
Nexus	(hiv or aids) **and** immune* and (human or verworve or menslike) **and** (s1&s2) and (milk or breast milk adj milk or human adj milk or moedersmelk or babvoeding* or feeding)	Full combination of keywords yielded 9 results which were irrelevant concerning the topic. When the part concerning pasteurization was left, 33 results were obtained which were mostly relevant concerning the topic.
ProQuest	(HIV or AIDS) **and** (milk or breast* or mother* milk or feeding)	When the full combination of keywords was used, no results were yielded. After leaving the part concerning pasteurization, 29 results were obtained.
Cochrane	(hiv or aids) **and** (milk or breast* or feeding)	When the full combination of keywords was used, no results were yielded.
SAePublications	(HIV or AIDS) **and** (heat or pasteuri* or steri* or boil*)	Full combination of keywords yielded only 1 result, after leaving the part concerning breast milk, 6 results were obtained.

Appendix 1.2

Table 1.2 Full-text copies excluded (including reason)

No	Author, year and title	Bottom line findings & Setting	Reason of exclusion (n=26)
Studies concerning the Holder method as heat treatment procedure only n= 9			
1.	Black (1996) Transmission of HIV-1 in the breastfeeding process *Journal of the American Dietetic Association,* 96(3):267-274. Jan-Jun	Concerning Holder pasteurization: destroys reverse transcriptase. Setting: unknown	Only Holder is mentioned as a pasteurization method.
2.	Chantry, C.J., Morrison, P., Panchula, J., Rivera, C., Hillyer, G., Zorilla, C & Diaz, C.(2000) Effects of Lipolysis or Heat Treatment on HIV-1 Provirus in Breast Milk *Journal of Acquired Immune Deficiency Syndrome,* 24(4):325-329.	The preliminary evidence suggests a inherent lipolytic activity of fresh breast milk is inadequate for destruction of HIV-1, bringing breast milk to a boil may result in decreased HIV-1 infectivity and breast milk cell-associated HIV-1 may not reflect plasma viral load. Nutritional value or possible bacterial contamination of milk treated in this manner was not assessed. Setting: Puerto Rico	The study mentioned only Holder pasteurization vs. fresh and lypolysis method to destroy HIV.
3.	Dhar, J., Fichtali, J., Skura, B.J., Nakai, S. & Davidson, A.G.F. (1996) Pasteurization efficiency of a HTST system for human milk *Journal of Food Science,* 61(3):569-595	Using a continuous flow HTST milk pasteurizer, human milk inoculated with *E.coli or S. aureus* was heated at 71C at different flow rates. All conditions completely inactivated both micro organisms and resulted in negative alkaline phosphatase activity indicating complete pasteurization. Heat processing of bovine milk at 71C at 5,9Ml/min resulted in retention of 30% GGTP activity. Pasteurization at 71C for 9,0 sec (12,3 Ml/min) resulted in retention of 74% of IgA, 75% IgG and 68% IgM.	Mentioned: a HSTS used in human milk banks, no Flash-heat (which is form of HTST) mentioned.

		Setting: unknown	
4.	Dialogue on diarrhoea (1995) HIV and infant feeding, *Dialogue on Diarrhoea,* 59:6. Dec-Feb.	Concerning heat treatment: Giving expressed sterilized breast milk is another option. Bringing breast milk to the boil or pasteurization (heating to 62,5 degrees centigrade for 30 minutes) kills HIV as well as other organisms. Setting: UK	Only Holder pasteurization mentioned.
5.	Lawrence, R.A. (1999) Storage of human milk and the influence of procedures on immunological components of human milk *Acta Peadiatrics,* 88:14-18.	The storage of human milk has impact on its constituents. These effects involve the storage container, heating, cooling and freezing the milk. Glass is the least destructive container. Milk can be safety refrigerated for 72h with little change. Freezing destroys cellular activity and reduces vitamins B6 and C. Boiling, destroys lipase and reduces the effect of immunoglobulin A and secretory immunoglobulin A. The nutrient value of human milk is essentially unchanged, but the immunological properties are reduced by various storage techniques. Setting: USA	Only Holder pasteurization mentioned.
6.	Morrison, P. & Greiner, T. (2000) Infant feeding choices for HIV positive mothers *Breastfeeding Abstracts,* 19(4):27-28. May.	Concerning heat treatment: mothers want to consider expressing and treating their milk to deactivate its HIV content before feeding to the infant. Unfortunately, UN guidelines were developed before research has been done to develop and test simple methods for doing, such as heating up the milk to a certain temperature or freezing. Milk banks utilize Holder sterilization (62,5 degrees for 30 min). Boiling will also inactivate the HIV and though it will destroy some components in the breast milk, boiled human milk remains more physiologically suited to the human infant than a formula prepared from animal milk.	Only Holder pasteurization mentioned.

		Setting: Zimbabwe	
7.	Ogundele, M.O. & Coulter, J.B.S. (2003) HIV transmission through breastfeeding: problems and prevention *Annals of Tropical Pediatrics,* 23:91-106	Concerning heat treatment: HIV is inactivated by pasteurization (62,5 C for 30 minutes) might be a practicable and affordable option in middle-income countries Setting: UK	Only Holder pasteurization mentioned.
8.	Orloff, S.L., Wallingford, J.C. & McDougal, J.S. (1993) Inactivation of Human Immunodeficiency Virus Type I in human milk: effects of intrinsic factors in human milk and of pasteurization *Journal of Human Lactation,* 9(1):13-17.	Pasteurization (62,5 C for 30 minutes) effectively inactivated the infectivity of both cell-free HIV-1 and HIV-1 infected cells by more than 5 logs and 6 logs respectively Setting: USA	Only Holder pasteurization mentioned (as used in milk banks).
9.	Silvestre, D., Ruiz, P., Martinez-Costa, C., Plaza, A. & Lopez, M.C. (2008) Effect of pasteurization on the bactericidal capacity of human milk *Journal of Human Lactation,* 1-6.Sept.	In all cases, pasteurization reduced the bactericidal capacity of milk versus untreated fresh milk. Human milk possesses antimicrobial activity that is lost in part as a result of thermal processing. Such bactericidal capacity is better preserved by low-temperature, long-time pasteurization. Setting: Spain	Concerning pasteurization in milk banks. Only Holder pasteurization mentioned.
Non-research report n = 13			
1.	Abrams, B. (2007) HIV, exclusive breastfeeding and weaning in sub-Saharan Africa: can flash-heating breast milk help bridge the gap? *Future HIV Therapy*. 1(3): 235-238.	More testing is needed concerning flash-heated breast milk to be a viable option. If flash-heated breast milk can be used safe, many babies could be saved from HIV infection Setting: USA	Narrative literature review. Non-research report.

2.	Anonymous (2006) Nutrition: Post-natal mother-to-child transmission of HIV and infant feeding practices: nutrition *Professional Nursing Today,* 10(6):38	Pretoria pasteurization mentioned as success full implementation to decrease MTCT of HIV and necrotising entero colitis in premature infants Setting: South Africa	Concerning PP but non-research report
3.	Coovadia, H.M. & Coutsoudis, A. (2001) Problems and advances in reducing transmission of HIV-1 through breast-feeding in developing countries *AIDScience.*1(4):1-12, Jul	Interventions to reduce breast-feeding transmission include heat treatment of expressed breast milk. Policymakers considered that expressing and heat treating breast milk is too difficult to be implemented on a large scale. But it can be implemented for working women. The Holder pasteurization has shown to destroy HIV while remaining most of the protective factors in the milk. Evidence exists for pasteurizing milk in a home setting (Pretoria Pasteuriation). Setting: South Africa	Narrative literature review. Non-research report.
4.	Foster, G. (1997) Realistic alternatives to breastfeeding in the HIV/AIDS era *Sexual Health Exchange,* 4 Available via: http://www.kit.nl/exchange/html/1997_4_realistic_alternatives.asp	Concerning heat treatment: mentioned heat treatment only once to pasteurize colostrum for 1st few days which may reduce neonatal infection. Setting: Zimbabwe	Concerning pasteurization but non-research report.

5.	Hartmann, S.U., Berlin, C.M. & Howett, M.K. (2006) Alternative modified infant-feeding practice to prevent postnatal transmission of human immunodeficiency virus type 1 through breast milk: past, present and future. *Journal of Human Lactation.* 22(1):75-88.	Comparison of the following methods: Holder pasteuriation, heat treatment, solar-powered pasteuriation, Pretoria pasteurization, boiling breast milk and microbicidal treatment. Heat treatment needs further research (especially in safety: potentially negative impact of heating/boiling on breast milk, feasibility and acceptability) Setting: USA	Narrative literature review. Non-research report.
6.	Jeffreys, B. (2000) New, simple local method for pasteurising HIV positive mother's breast milk *MRC News,* 31(4):23-24. Aug.	Discussion possibility PP. Setting: South Africa	Concerning PP but non-research report.
7.	Jeffery, B. (2001) Pretoria pasteurization *SAJOG,* 89	Possible solution to Mother-to-Child transmission of HIV through breast feeding could be Pretoria Pasteurization. Tests have shown that this is an effective method for killing the HIV, and the milk can safely be given to the infant without fear of transmission of the virus. Setting: South Africa	Concerning PP but non-research report.
8.	Morrison, P. (2003) Pasteurized breastmilk as a replacement feed for the babies of HIV infected mothers. ProNUTRITION, http://www.pronutrition.org/files/Pasteurized%20Breastmilk.txt	Pasteurization of breast milk at home, using simple equipment is safe and possible. Expressed breast milk should be stored in clean, covered containers. 2 types of pasteurization: flash-boiling and Pretoria pasteurization. Baby can be fed pasteurized milk by cup, spoon or (sterilized)bottle. Setting: Zimbabwe	Narrative literature review. Non-research report.
9.	Rollins, N., Meda, N., Becquet, R., Coutsoudis, A., Humphrey, J., Jeffrey, B., Kanshana, S., Kuhn, L., Leroy, V., Mbori-Ngacha, D., Mcintyre & J., Newell, M-L.	Concerning heat treatment: *Feasibility and acceptability* of heat treatment was seen as too time consuming to be a practical alternative of breast feeding. Expressed breast milk was strongly	Narrative literature review. Non-research report.

	(2004) Preventing postnatal transmission of HIV-1 through breastfeeding: modifying infant feeding practices *Journal of Acquired Immune Deficiency Syndrome.* 35(2):188-195. Feb.	rejected by a number of participants because it was strongly associated with stillbirths, infant deaths of pre-term births. Nurse counsellors mentioned that mothers should provided with information concerning teaching hand expressing. General: importance of formative research to develop intervention to improve counselling and changing customary feeding practices. Setting: UK	
10.	Schultz, M. (2001) Clinical: Infant milk supplements and weaning *SA Pharmaceutical Journal incorporating Pharmacy Management,* 30-37.Jun.	Weaning and infant formula feeding are possible infant feeding options. Setting: South Africa	Non-research report.
11.	Tully, M.R (1999) Is pasteurized mother's own or donor milk the answer to the HIV crisis? *Journal of Human Lactation*. 15:345-346.	Concerning Pasteurisation correctly applied heat treatment of expressed breast milk can reliably inactivate HIV within the milk. It is easy to implement for motivated mothers but avoidance of suckling the infant and contending with family and community pressures are serious considerations for success. Pretoria Pasteurization is a useful method for feeding pre-term infants born to HIV infected mothers in an institutional setting but its use in a domestic setting and for term infants requires further investigation. It may have a valuable role as an alternative to exclusive breastfeeding during times of increased risk, such as mastitis and cracked or bleeding nipples. Setting: USA	Narrative literature review. Non-research report.
12.	WHO (2008) HIV transmission through breastfeeding: a review of available evidence- an update	Heat-treated EBM is a method endorsed by WHO to reduce postnatal transmission of HIV. Pretoria Pasteurization and Flash-heat can effectively inactivate HIV virus in breast milk. It may be	1/2 page concerning heat treatment as alternative method but non-research report.

	from 2001-2007. *WHO*, Geneva, Switzerland *WHO*:58	feasible for HIV positive mothers in Zimbabwe. It could be useful after a period of exclusive breast feeding. Pasteurization seems difficult to implement on a large scale, it requires access to developed infrastructure and safe practices, which can be difficult in resource-poor settings. Setting: unknown	
13.	WHO (2007) HIV and infant feeding update Based on the Technical Consultation held on behalf of the Inter-agency Task Team (IATT) on Prevention of HIV Infection in Pregnant Women, Mothers and their Infants Geneva, 25-27 October 2006 *WHO,* 1-14.	Concerning heat treatment of EBM: While no longer considered a main infant feeding option, heat-treatment of expressed breast milk may be feasible for some women, especially after the baby is a few months old and during the transition from exclusive breastfeeding to replacement feeding. The only method recommended by WHO at home is boiling. However, other methods that may be easier and quicker, while still safe, are currently being tested for feasibility. Setting: unknown	Document regarding the meeting held in October 2006 with updated recommendations and explanation of key points. Non-research report.
Duplicates n=3			
1.	Israel-Ballard, K., Donovan, R., Chantry, C.J., Coutsoudis, A., Sheppard, H., Sibeko, L. & Abrams, A. (2007) Flash-Heat inactivation of HIV-1 in human milk: a potential method to reduce postnatal transmission in developing countries. *Journal of Acquired Immune Deficiency Syndrome,* 45(3):318-323.Jul.	FH can inactivate HIV in naturally infected breast milk from HIV positive women. Field studies are urgently needed to determine the feasibility of in-home FH breast milk to improve infant health while reducing postnatal transmission of HIV in developing countries. Setting: South Africa	Duplicate of: Israel-Ballard, K.A. (2007:1-97) Demonstrating the Safety of Flash-heated Breast Milk: A Potential Infant Feeding Option for HIV Positive Mothers in Developing Countries Berkely: University of California. Dissertation

2.	Israel- Ballard, K.A., Abrams, B.F., Coutsoudis, A., Sibeko, L.N., Cheryk, L.A. & Chantry, C.J. (2008) Vitamin content of breast milk from HIV-1 infected mothers before and after flash-heat treatment *Journal of Acquired Immune Deficiency Syndrome,* 48(4):444-448. Aug.	The percentage remaining after FH suggests that most vitamin concentrations are retained after heating. FH may be a practical and nutritious infant feeding method for mothers in developing countries. Setting: South Africa	
3.	Israel-Ballard, K., Coutsoudis, A., Chantry, C.J., Sturm, A.W., Karim, F., Sibeko, L. & Abrams, B. (2006) Bacterial safety of flash-heated and unheated expressed breastmilk during storage. *Journal of Tropical Pediatrics,* 52(6):399-405.	FH is capable to eliminate pathogenic and non-pathogenic bacteria, and 8h storage period outside the refrigerator does not result in a significant decrease of bacteria. FH is a simple EBM pasteurization method that could be a safe infant-feeding option for mothers in need of breast milk modifications, such as HIV positive mothers in developing countries where resources such as refrigerators are lacking. Setting: South Africa	
Irrelevant studies: studies not specific to breast milk/breast feeding/ studies not specific to heat treatment/pasteurization *n= 1*			
1.	Draper, B. & Abdullah, F. (2008) A review of the prevention of mother-to-child transmission programme of the Western Cape provincial government 2003-2004 Issues in public health: SAMJ forum *South African Medical Journal,* 98(6):431-434. June.	New research has shown improved efficacy with a regimen of single-dose nevirapine combined with a short course of zidovudine to both mothers and infants. It has also become apparent that HIV-positive pregnant women who need ART for their own health should receive it during pregnancy. The provincial PMTCT programme has made significant strides in this direction and has shown that it is possible to move forward with new approaches to prevent MTCT in South Africa. Setting: unknown	Nothing specific mentioned to heat treatment/pasteurization