How Many Cs in NICU?

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Submitted to the University of Technology, Sydney
in fulfilment of requirements for the degree of
Doctor of Philosophy

2013
I certify that the work in this thesis has not previously been submitted for a degree nor
has it been submitted as part of requirements for a degree except as fully acknowledged
within the text.

I also certify that the thesis has been written by me. Any help that I have received in my
research work and the preparation of the thesis itself has been acknowledged. In
addition, I certify that all information sources and literature used are indicated in the
thesis.

Lynn Sinclair
10 September 2013
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Peer-Reviewed Publications and Conference Presentations

Peer-Reviewed Publications


Conference Presentations


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<th>Description</th>
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<tbody>
<tr>
<td>ACT</td>
<td>Australian Capital Territory</td>
</tr>
<tr>
<td>AIHW</td>
<td>Australian Institute of Health and Welfare</td>
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<tr>
<td>ANZNN</td>
<td>Australia and New Zealand Neonatal Network</td>
</tr>
<tr>
<td>AQP</td>
<td>Aquaporin</td>
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<tr>
<td>CLD</td>
<td>Chronic lung disease</td>
</tr>
<tr>
<td>CNC</td>
<td>Clinical nurse consultant</td>
</tr>
<tr>
<td>CNRG</td>
<td>Cochrane Neonatal Review Group</td>
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<tr>
<td>CONSORT</td>
<td>Consolidated Standards of Reporting Trials</td>
</tr>
<tr>
<td>CP</td>
<td>Cerebral palsy</td>
</tr>
<tr>
<td>CPG</td>
<td>Clinical practice guidelines</td>
</tr>
<tr>
<td>CRCT</td>
<td>Cluster randomised controlled trial</td>
</tr>
<tr>
<td>CRIB</td>
<td>Clinical Risk Index for Babies</td>
</tr>
<tr>
<td>CTC</td>
<td>Clinical Trials Centre</td>
</tr>
<tr>
<td>DOI</td>
<td>Diffusion of Innovations</td>
</tr>
<tr>
<td>DSMC</td>
<td>Data and Safety Monitoring Committee</td>
</tr>
<tr>
<td>EBM</td>
<td>Evidence-based medicine</td>
</tr>
<tr>
<td>EBP</td>
<td>Evidence-based practice</td>
</tr>
<tr>
<td>ECW</td>
<td>Extracellular water</td>
</tr>
<tr>
<td>EoC</td>
<td>Essentials of Care</td>
</tr>
<tr>
<td>fMRI</td>
<td>functional magnetic resonance imaging</td>
</tr>
<tr>
<td>HIPI</td>
<td>Humidity in Incubators for Preterm Infants</td>
</tr>
<tr>
<td>HREC</td>
<td>Human research ethics committee</td>
</tr>
<tr>
<td>ICC</td>
<td>Intracluster correlation coefficients</td>
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<tr>
<td>ID</td>
<td>Identification</td>
</tr>
<tr>
<td>IVH</td>
<td>Intraventricular haemorrhage</td>
</tr>
<tr>
<td>MRN</td>
<td>Medical record numbers</td>
</tr>
<tr>
<td>NEC</td>
<td>Necrotising enterocolitis</td>
</tr>
<tr>
<td>NHMRC</td>
<td>National Health and Medical Research Council</td>
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<tr>
<td>NICU</td>
<td>Neonatal intensive care unit</td>
</tr>
<tr>
<td>NICUS</td>
<td>Neonatal Intensive Care Units</td>
</tr>
<tr>
<td>NSW</td>
<td>New South Wales</td>
</tr>
<tr>
<td>Acronym</td>
<td>Term</td>
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<td>-------------------------------------------</td>
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<tr>
<td>PARiHS</td>
<td>Promoting Action on Research Implementation in Health Services</td>
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<tr>
<td>PDA</td>
<td>Patent ductus arteriosus</td>
</tr>
<tr>
<td>PET</td>
<td>Positron emission tomography</td>
</tr>
<tr>
<td>PICO</td>
<td>Patients, intervention, comparator and outcomes</td>
</tr>
<tr>
<td>PSANZ</td>
<td>Perinatal Society of Australia and New Zealand</td>
</tr>
<tr>
<td>PSN</td>
<td>Pregnancy and Newborn Services Network</td>
</tr>
<tr>
<td>PVL</td>
<td>Periventricular leukomalacia</td>
</tr>
<tr>
<td>qEEG</td>
<td>quantitative electroencephalography</td>
</tr>
<tr>
<td>QUOROM</td>
<td>Quality of Reporting of Meta-Analyses</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>SAE</td>
<td>Serious adverse event</td>
</tr>
<tr>
<td>SCAN</td>
<td>Social cognitive affective neuroscience</td>
</tr>
<tr>
<td>SCARF</td>
<td>Status, certainty, autonomy, relatedness, fairness</td>
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<tr>
<td>SCARF-SA</td>
<td>SCARF-Self-Assessment</td>
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<tr>
<td>SNAPPE-II</td>
<td>Score for Neonatal Acute Physiology—Perinatal Extension</td>
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<tr>
<td>SPIRIT</td>
<td>Standard Protocol Items: Recommendations for Interventional Trials</td>
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<tr>
<td>TEWL</td>
<td>Transepidermal water loss</td>
</tr>
<tr>
<td>TGA</td>
<td>Therapeutic Goods and Administration</td>
</tr>
<tr>
<td>TMC</td>
<td>Trial management committee</td>
</tr>
<tr>
<td>TMS</td>
<td>Transcranial magnetic stimulation</td>
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Abstract

Neonatal clinicians are challenged to ensure practice is evidence based and health outcomes are positive, which necessitates ongoing innovation and change. In the neonatal intensive care unit (NICU), assessment of the effectiveness of both new and existing interventions is required to reduce the burden of illness for extremely preterm infants and their families. The initial focus of the doctoral work outlined within this thesis was the investigation of the use of incubator humidity in the care of premature infants. My original doctoral plan was to undertake a randomised controlled trial in order to produce robust evidence to guide clinicians in humidity use and reduce the existing variability in practice. The doctoral work evolved to include a review of the broad literature that examines the physiological and historical context of humidification practices; a systematic review of randomised controlled trials that identifies a lack of research evidence to direct practice; a survey of humidification practices in NICUs across Australia and New Zealand that highlights the extent of the diversity in day-to-day practices; a single centre audit that was unable to detect any patterns between incubator humidity and neonatal health outcomes, but did reveal diversity in practice; and, the development of a protocol for the randomised controlled trial required to test the effect of different levels and duration of humidity and its effect on clinically important outcomes. The final chapters build on these findings and explore the kind of workplace cultures that are required to maximise the generation of meaningful evidence and the likelihood that clinicians would use this evidence to inform practice. The final chapter also explores the potential of contemporary social, cognitive, affective neuroscience for providing causal explanations for interventions such as transformational practice development (tPD) as well as providing pointers to additional strategies for creating more positive workplaces for clinicians and families.
Chapter 1: C’ing the Status of the Subject: Need for Change

Most of us who work in neonatal paediatrics are distressingly familiar with the sight of a small infant surrounded by a fog of vapour within a closed tent or incubator. This situation perhaps symbolises the present status of this subject, which is essentially a very small body of facts enveloped in a misty atmosphere of speculation, which is walled off from its surroundings by a rigid container of prejudice. (Clement Smith 1955, p. 2051)

The above quote was published in 1955; however, after spending 30 years as a clinician and several years of doctoral work, I believe that it could have just as easily been written in 2013. The work described within this thesis captures the knowledge generated and learning achieved as I undertook a series of scholarly activities aimed at developing robust research evidence in relation to the use of humidification in the care of extremely preterm infants. My original doctoral plan involved collaboration with a multidisciplinary team in the generation and implementation of a randomised controlled trial (RCT) to identify optimal levels and duration of humidification. However, circumstances and challenges shaped my doctoral journey such that it became one of discovery related to:

- the status of the subject of humidification within the neonatal intensive care unit (NICU) and the need for change;
- the very small body of facts that form the evidence base for humidification practices;
- the rigid container that is the practice context in which diverse humidification practices evolve and exist;
- the prejudice with which those working in NICUs work to maintain the status quo;
- the complexities associated with clearing the fog of vapour surrounding local practices and outcomes;
- additional complexities associated with meaningful collaboration for clearing the misty atmosphere of speculation through the generation of robust research evidence and its implementation into practice; and
- the very real challenges of uncovering better ways of engaging clinicians in creating the kind of workplace cultures that are self-sustaining and effective.
This introductory chapter outlines my doctoral journey, provides the background to and rationale for undertaking the work, introduces the world of extremely preterm infants and describes the challenges clinicians face in providing evidence-based care for this population. In doing this, the chapter seeks to capture the ways that the focus of my research, and indeed my entire doctoral journey, evolved in relation to the major challenges that I encountered, and the decisions taken in response to those challenges. I conclude by providing a précis of what the reader will find within each chapter.

1.1 Background to the Work of the Thesis

Contemporary health care systems promote safe, effective, evidence-based practice (EBP) that meets the needs of patients and families and clinical governance. As clinical excellence and best practice are never static, care practices need to be able to evolve because the rate at which researchers produce evidence is increasing rapidly. Consequently, within New South Wales (NSW), this challenges health care professionals every day to keep up to date with Ministry of Health and local policy initiatives and meet accelerating demands for quality care as identified through research. This requires clinicians to review current practices that may no longer be appropriate or clinically effective, critically appraise the literature, incorporate the evidence into clinical decision making and, where appropriate, undertake research to develop new therapies. Although there is increasing recognition by clinicians that the highest level of evidence available should guide decision making to ensure optimal patient outcomes, adoption of new policies and practices is highly variable, and gaps and delays that inhibit the timely uptake of research are a reality.

The need for ongoing innovation and change is thus a given in today’s health care organisations. Of particular relevance to the work outlined here is the recent restructure of health services in NSW, Australia, and a new statutory health corporation known as NSW Kids and Families established in 2012. NSW Kids and Families champion the health interests of children and young people, whether they are at home, in the community, in or out of hospital. The corporation includes health services for babies, children, adolescents, mothers, parents and families. The restructuring of services followed earlier publications, including Investing in the Early Years (Council of
Australian Governments 2009) and several high-profile reports on a broad range of health, development and wellbeing indicators, such as *A Picture of Australia’s Children 2009* (Australian Institute of Health and Welfare 2009). This report revealed that an estimated 8% of Australian children had a disability in 2003 and, of these, half had profound or severe core activity limitations. The prevalence of disability had increased from 5.3% in 1981 to 8.3% in 2003, and neonatal problems were identified as one of the leading causes of burden of disease (Begg et al. 2007). The document *Investing in the Early Years* urges all health care professionals to assist in reducing the incidence and extent of disability where possible.

Extreme prematurity (birth before 28 completed weeks of gestation) contributes significantly to the burden of illness; hence, evaluating the effect of interventions on neonatal health outcomes has become a health care priority. Although mortality following extreme prematurity has greatly reduced over time, there has been no corresponding reduction in morbidity (Costeloe et al. 2000; Johnson et al. 2009; Roberts et al. 2010; Stoll et al. 2010; Vanhaesebrouck et al. 2004). Morbidities include chronic lung disease (CLD), late-onset sepsis, severe intraventricular haemorrhage (IVH) and necrotising enterocolitis (NEC), and each is an independent risk factor for poor long-term health and adverse neurological, motor, cognitive and sensory impairments (Saigal & Doyle 2008; Stoll et al. 2004; Stoll et al. 2010). The underlying mechanisms responsible for adverse neurodevelopmental outcomes include brain injury and altered brain development, including impaired regional brain development (Inder 2013). Risk factors for altered regional brain development in the preterm infant differ from those of conventional brain injury and are influenced by the infants’ experiences within the NICU (Inder 2013). In addition, the increase in numbers of infants at risk for poor long-term health affects the finite resources of our health care and educational systems and has workforce implications for the future. Consequently, increasing survival of the most immature infants has challenged clinicians to assess the effects of the NICU and the efficacy not only of new treatments but also of existing interventions to ensure positive health outcomes.
1.2 My Experiences and Motivation as a Clinician

The work of this thesis arose primarily from my practice concerns about the thermal management of a subgroup of infants: those born extremely preterm. Observations of care revealed that, on many occasions, extremely preterm infants admitted to the NICU were exposed to prolonged periods of hypothermia (body temperature less than 36 °C) during the first few hours and sometimes days after birth. Hypothermia compromises already stressed and immature body systems and is a known independent risk factor for mortality and morbidity in preterm infants (Costeloe et al. 2000; Oxley & Lyon 2001; Parry, Tucker & Tarnow-Mordi 2003). Since this NICU provided care for the greatest number of extremely preterm infants born in NSW (ANZNN 2004), the finding was of considerable concern to me.

Achievement and maintenance of a normal body temperature is essential for survival, and thermal management is a key role of the neonatal nurse. In my previous nursing experience, management of extremely preterm infants included the provision of incubator humidity in an attempt to reduce evaporative heat and water losses and improve thermal stability and fluid balance. I had witnessed improved thermal stability following humidity use in clinical practice. However, the humidification of incubators was not a recognised practice within this particular NICU.

Adopting a collaborative approach, I discussed the subject of incubator humidity with the local multidisciplinary team. Discussion revealed little support for and much criticism of humidity use. In particular, many clinicians voiced concern about the potential for increased risk of nosocomial infection within the warm, moist microenvironment supplemental humidity created. Subsequent consultation with neonatal colleagues in the wider clinical arena revealed that all other NICUs in NSW routinely used incubator humidity in the management of preterm infants, although some variation in use was apparent. Reflecting on the incidence and severity of hypothermia in our NICU and the statewide discussions regarding peer practices, I was motivated to seek evidence to determine best practice that may positively influence neonatal health outcomes.
I engaged a small multidisciplinary group, and together we searched and reviewed the medical literature. Our aim was to determine current knowledge and level of evidence for incubator humidity use, and then utilise it to develop clinical practice guidelines (CPG) with a view to introducing incubator humidity as a standard of care within the NICU. It became apparent that, although anecdotally humidity use was increasing within NICUs, evidence for use was based primarily on observational and physiological data. The studies described short-term outcomes of improved thermal stability and fluid and electrolyte balance; however, optimal levels and duration of humidification were unclear, and evidence of the effect of humidification on health outcomes appeared lacking. Further, we could find no recent evidence to support or refute the concern that humidification increased sepsis risk; surely, it remained a possibility nonetheless.

Existing practices within the NICU were out dated, steeped in tradition, based on local experience and opinion, and had become routine. The assumptions were that there had been adequate assessment of the efficacy and safety carried out previously, so there was no impetus for change. Challenging such beliefs once a practice is well established can prove difficult, and limited opportunities were available for nurses to initiate change within this practice environment. Further, this NICU had a reputation for disruptive clinician behaviour; vertical and horizontal violence was the norm. I had witnessed these behaviours, staff and parent responses to them, and the toxic atmosphere they created. There was a recognised need by some clinicians to overcome local challenges related to interpersonal conflicts and to review existing practices and align them with contemporary evidence.

Evaluation of existing thermal management strategies highlighted deficits and challenged existing assumptions and behaviours within the NICU. All members of the small multidisciplinary group recognised the need for change. Appraisal of the evidence led to a group decision to provide humidity for all infants less than or equal to 28 weeks gestation during the first week of life; a longer duration could not be agreed upon. With the assistance of the infection control team, an ongoing audit process would closely monitor progress and detect early any complications of use, including sepsis rates. We developed the CPG based on the best available evidence, complete with education and implementation plans. A challenging time ensued because there was little support for
the proposed practice change outside the review group and tensions existed between clinicians. Several clinicians strongly contested the practice change, and incubator humidity became an emotive subject. Eighteen months later, following intensive discussions, incubator humidity ‘officially’ became a standard of care in the management of preterm infants within the NICU. However, humidification practice appeared to vary from day to day, infant to infant and clinician to clinician because of the lack of consensus on use. Those concerned about sepsis risk did not humidify the environment when providing care for extremely preterm infants.

It is important to note that this situation occurred against a backdrop of an organisation in turmoil. The effects of an organisation undergoing restructure and constant change contributed to an unpredictable, complex and stressful working environment. Additionally, there was increasing complexity and acuity of patient care, increasing demand for EBPs that were both clinically and cost effective, and increasing consumer expectations of positive health care outcomes for the most preterm infants in an era when nursing shortages, inappropriate skill mix, finite resources and poor leadership were a reality.

Based on my clinical experiences, the work outlined within this thesis began with a plan to generate robust evidence in one area of practice within the NICU: the provision of incubator humidity in the management of preterm infants. The following section presents my experiences as a researcher throughout my doctoral journey, my philosophical viewpoint, the decisions made and how these revealed an alternative view of the health care world.

1.3 My Experiences and Motivation as a Researcher

This research journey began with my rather naive search for certainty—an elusive concept, as I was to discover. Familiar with quantitative methodology and the RCT, I was very keen to put my previous learning to good use, and to design and conduct an RCT as part of my thesis. There is general acceptance that evidence of efficacy or effectiveness of interventions demands an RCT, preferably aggregated into systematic reviews of several RCTs. Therefore, I was certain that my research questions could be
answered using this methodology; this made perfect sense, was logical and, for me, easy to understand because it sat comfortably with my research training and preferences. Chapters 2 through 6 demonstrate the systematic approach initially taken to achieve this aim. However, as my doctoral journey evolved it took a different path—one in which I gradually realised that an RCT was not going to be possible and that my search for certainty was more complicated and far more elusive than I had first thought.

I was disappointed that I could not conduct an RCT as part of my thesis. On reflection, this is when my learning began—when I left behind what was familiar. I spent a great deal of time reflecting on my experiences as a neonatal nurse and the challenges at the heart of practices within NICUs. These reflections challenged my initial assumptions concerning the quality and safety of care provided to preterm infants nursed in humidified environments. My learning also challenged the extent to which conventional means of generating robust evidence and the extent to which my initial views about research evidence and practice change (those of a post-positivist) were useful. Further, discussion with my supervisors and my reading of the literature about the challenges of transferring research evidence into positive patient outcomes, identifying the attributes of a workplace that contribute to its effectiveness (or do not) and understanding the drivers of human behaviour captured my attention and sparked my curiosity. This curiosity led me to the work of implementation science, contemporary neuroscience and the evolving field of neuroleadership, and practice development. The result was that my new understandings influenced both the focus of the work and my way of viewing the health care world.

The work then evolved into a thesis that is exploratory and descriptive—that discusses the challenges encountered and explores the complexities of designing a clinical trial that investigates the effect of humidity on neonatal health outcomes in the face of a paucity of robust research, wide practice variation and divergent clinician opinion. The thesis outlines my evolving understanding of a variety of factors that researchers need to consider and work with constructively when and if RCTs are required—contextual, social and individual factors that I have come to believe determine, not only the feasibility and integrity of the trial itself, but also the extent to which findings will ultimately influence practice. I have come to realise that any attempt to generate and
utilise meaningful research evidence requires us to deal with the realities that surround the profound challenges of engaging in change, working with and within complex and highly resistant contexts, seeking certainty in uncertain clinical settings, and working within complex multidisciplinary teams.

The thesis concludes by synthesising work from contemporary neuroscience with transformational practice development that has the potential to create effective work cultures.

In summary, this work began because I was passionate about providing the best possible care to preterm infants and their families within the NICU. Roach (1987) defined the five Cs of caring—compassion (sharing in the world of the patient), conscience (sensitive awareness to moral and ethical dilemmas), competence (appropriate knowledge and skill), confidence and commitment (a steadfastness of purpose and devotion to the needs of the other)—and she later added a sixth: comportment (the way or manner in which one conducts oneself) (Roach 1997). Roach’s Cs reflect the values that should be at play either implicitly or explicitly in care provision. However, during my research journey, I encountered several other Cs that are crucial in determining the extent to which clinicians can provide the best possible care as they affect, either positively or negatively, the Cs outlined by Roach. These additional Cs are certainty, change, context, characters, complexity and culture.

The following section provides a précis of each chapter.

1.4 Organisation of the Thesis

1.4.1 C’ing the status of the subject: Need for change

This introductory chapter has outlined my doctoral journey and provided a background to and a rationale for undertaking the work of the thesis. The chapter introduced the extremely preterm infant and highlighted the challenges of providing EBP for this vulnerable population, for which there is now pressing need if we are to improve long-term health outcomes. The chapter then considered my workplace, my experiences in the NICU, and the challenges of implementing incubator humidity—an intervention that
is fraught with controversy and for which there is little robust evidence to guide clinical decision making. The chapter then reflected on my role as a researcher and explained how the work evolved and changed focus following the realisation that, because of the major challenges encountered and the decisions made, I was unable to conduct the RCT to establish clear evidence around humidification use as planned.

The chapter also made explicit how reflecting on the fundamental issues underpinning patient care increased my awareness of the interplay between the multiple factors that may influence decisions regarding patient care practices within NICUs. I now believe knowledge of the factors at play is essential when considering trial design to increase the likelihood of clinician compliance with the trial protocol and, later, the implementation of findings into practice. My evolving understanding of this complexity led to my exploration of the attributes required to enable an effective workplace culture and, especially, the drivers of human behaviour that provide insight into ways of improving relationships within the practice environment.

The following six chapters reflect the systematic approach taken to gain a deeper understanding of what is known about incubator humidity and its use in the management of extremely preterm infants, identify important outcome variables and gaps in the literature that could help refine the research questions, and determine what a future trial should look like. This methodical approach included a broad review of the literature, a systematic review of RCTs, an exploration of humidification practices across NICUs and neonatal nurses’ views and opinions of use, and an investigation of the effects of introducing incubator humidity on short-term health outcomes in one NICU. Collectively, this work informed the development of the protocol for the RCT. Each chapter includes a section that provides the reader with insight into my reflections: the learning and the critical questions posed that influenced my thinking and decision making along the way.

1.4.2 C’ing the rigid container: Practice in context

Chapter 2 provides a broad review of the published literature relating to the evolution and use of the humidified incubator. The chapter is presented in three sections. The first section investigates the evolution of humidification practices in two different practice
contexts: France and the United States. The second section explores the vulnerabilities of the increasing extremely preterm infant population that relate to humidity use. Physiological evidence confirms the role of high levels of humidity (greater than or equal to 80%) in reducing water and heat loss from the skin, and that clinicians humidify incubators to promote thermal stability and fluid balance. However, prolonged high-level humidity use might delay skin maturation, the effect of which is unclear. The final section of the chapter reflects on contemporary issues related to humidity use: the anecdotal evidence of increasing humidity use, the lack of clear guidance on the practicalities of use such as optimal levels and duration of humidity of infants of varying gestational ages, and the lack of robust evidence of its effect on clinically important health outcomes, in particular, whether incubator humidity contributes to sepsis rates.

1.4.3 C’ing the very small body of facts: Research evidence in context

Chapter 3 presents the published protocol for, and reports the findings of, the full systematic review of RCTs, which assessed the level of existing evidence of the effectiveness of humidification on neonatal health outcomes. The reviews within the Cochrane Database of Systematic Reviews are considered high quality because of a comprehensive peer review process and adherence to rigorous methodology; therefore, I decided to conduct a systematic review using the methods of the Cochrane Collaboration. The review confirmed the findings of the broad review of the literature: optimal levels and duration of incubator humidity are unknown, benefits and risks are unclear, and there is little evidence of its effect on short or longer term health outcomes. The chapter continues by discussing systematic review methodology and reflecting on the challenges I encountered during the process of review. These challenges, which included failure to achieve consensus on the outcome of the review, mean that the full review remains, at this time, unpublished.

Given the lack of evidence to guide practice and my own experiences of incubator humidity use within my workplace, I was curious to know how clinicians in other NICUs used humidity and whether the context of the practice environment influenced
decisions regarding its use. I hypothesised that there would be a diversity in practice across centres.

1.4.4 C’ing the prejudice in practice: Characters in context

Chapter 4 presents the findings of a telephone survey of incubator humidity practices and nurses’ views of humidity use in NICUs across Australia and New Zealand, which were published in a peer-reviewed journal. The survey had three aims: to determine how clinicians use humidity in their workplace and what influences its use, to explore views and beliefs about humidity use, and to identify the extent to which clinicians use CPGs to inform practice. The chapter begins by presenting the published paper that established that all NICUs used incubator humidity and, as anticipated, had wide variation in practice. Greatest variation was evident in the gestational age range of infants who received humidity as an intervention and in the duration of use; this variation was evident both across and within NICUs.

The chapter then presents a more detailed description of the methods used and the participants’ views and experiences of humidity use that were not included in the published paper due to word limitation. The chapter presents the findings of the survey within four major themes: an overarching theme of uncertainty in the practice environment, and the themes working with humidity in practice, working with evidence and guidelines and context of practice. One striking and ubiquitous finding was that humidification practices (and others) are personality driven and independent of an existing CPG. The lack of consensus among both neonatologists and nurses, and the resultant inconsistencies in practice, contributed greatly to uncertainty, confusion and frustration within the practice environment. The chapter explores the effect of inconsistency on clinicians and parents within the NICU and highlights the need to consider the effect the findings had on the potential to complicate the design and execution of the proposed trial.

The introduction of incubator humidity in my workplace provided the opportunity to compare a group of infants who received humidity with another group of infants that did not.
1.4.5 C’ing the fog of vapour: Complexity of intervention = outcome links

Chapter 5 presents the findings from a retrospective audit that compared a group of 109 infants nursed in humidified incubators with a previous cohort of 102 infants cared for in non-humidified incubators (before the practice change). This audit had three main aims: to describe which variables are important when investigating the effect of humidity on extremely preterm infants, to determine an appropriate sample size for the RCT and to compare current practice with that detailed within the local CPG to determine to what extent clinician opinion and the practice environment influenced humidification practices and, therefore, patient care.

The audit was inconclusive because it revealed two non-comparable infant groups: infants in the humidity group were more preterm, of lower birth weight and therefore at increased risk for associated morbidities than the infants in the non-humidified group. Similar to the results of the survey, the audit found individual beliefs about the benefits and risks of humidity use complicated practice; clinicians who did not support the use of humidity did not use it. The chapter discusses the implications of the findings for the proposed trial.

1.4.6 C’ing the misty atmosphere of speculation: The complexity of robust RCTs

Chapter 6 presents a draft protocol for the Humidity in Incubators for Preterm Infants (HIPI) Trial—a multicentre cluster randomised controlled trial (CRCT) that investigates the effect of incubator humidity on neonatal health outcomes. The chapter reveals what the trial might look like and discusses why, given the complex and dynamic nature of the NICU context and the challenges associated with knowledge generation, it was not possible to conduct the trial. The chapter then provides a critical analysis of the chosen methodology and questions the feasibility of a large multicentre trial, given the inconsistencies in practice, the complexity of clinical contexts and the individuals involved. The chapter concludes by drawing together key findings and lessons learnt, and suggests the need to acknowledge the effect of interpersonal relationships on local
culture, clinician wellbeing and family care, to seek to understand what constitutes an effective workplace culture, and to determine what drives human behaviour and how individuals relate to each other.

1.4.7 C’ing a way forward: Seeking to build more effective workplace cultures

Chapter 7 reflects on my research journey and draws together the thesis findings. The major finding is the importance of the practice environment or context on knowledge generation and utilisation, and patient care. The chapter raises awareness of the contextual realities that exist within the NICU environment, the relationships among the myriad of characters that make up the multidisciplinary team responsible for the care of infants and families, and the difficulties that arise when multiple characters seek certainty in the face of overwhelming complexity. Given this, the chapter seeks to understand more about how context contributes to workplace culture and how to determine what an effective workplace culture might look like and provides a critical exploration of the NICU context in light of what is known about effective workplace cultures.

1.4.8 C’ing a way forward: The complexity of working as, and with, human beings; seeking to build healthier relationships

Chapter 8 presents an examination of recent work in the field of contemporary neuroscience that identifies emotion as the primary driver of human behaviour and points to the realities surrounding intrapersonal and interpersonal processes and their impact on the social processes at the level of care provision. Neuroscience suggests strategies to reduce the impact of emotions on the individual and on others. Building on this work, the chapter introduces the evolving field of neuroleadership that suggests how the five domains of the SCARF® model (Status, Certainty, Autonomy, Relatedness and Fairness) affect whether individuals feel threatened or rewarded in social settings and therefore the degree to which they are able to collaborate effectively. Finally, the chapter explores how this literature might explain why approaches that create effective workplace cultures such as transformational practice development (tPD) enable
clinicians to develop healthy relationships, improve their practice environment and the care they provide.
Chapter 2: C’ing the Rigid Container: Practice in Context

The Evolution of Arguments for and against the Humidified Incubator in Contemporary NICUs

2.1 Chapter Overview

This chapter presents a broad overview of the large body of literature that informs the current clinical debate on the humidification of incubators in NICUs. The review sought to determine the state of the knowledge on incubator humidity use, define optimal levels and duration, identify potential benefits and risks, and determine the effect of humidity on clinically important neonatal health outcomes. The literature paints an interesting picture of the early drivers of humidity use and the physiological bases of the arguments for its use.

However, what the literature does not provide is a clear way forward for clinicians seeking to introduce humidity, or generate research evidence to guide its use. For instance, the several decades of writing and research have failed to provide clarity or consistency on specific levels or duration of humidification for premature infants, and leave clinicians unsure about suggested complications such as its potential link to rates of nosocomial sepsis in extremely preterm infants. Further, the literature review provides few details to inform the development of an RCT in terms of designing specific interventions and questions about which variables relevant to the use of incubator humidity should be included in an RCT that seeks to provide clear evidence to inform practice.

The chapter is organised into three sections. The first section explores the origins of the infant incubator in two very different contexts and discusses the evolution of humidification practices and the evidence that informed decision making over time. This historical account forms a basis for an analysis of the processes and politics of practice change that I will address later in the thesis when considering how to translate knowledge and innovation into practice. The second section of the chapter outlines the
critically important shifts in the characteristics of the population of infants cared for within NICUs over recent decades and the challenges this has posed for neonatal clinicians. This section also explores the vulnerability of the extremely preterm infant’s physiological state as it relates to humidity use. The third section reflects on contemporary issues and questions regarding incubator humidity, my learning and what the work of the chapter means for the proposed study.

On returning to this chapter towards the end of my thesis journey, I realised that it was lengthy and quite detailed. I reflected on this and reviewed my journal notes from that time. I now believe that this reflected my search for certainty, my need to feel certain that, working at the doctoral level, I was familiar with and understood all literature that might be relevant to the use of humidified incubators and to describe and share what is known; this is something we do when we are searching for certainty. Acknowledging this desire for certainty as a human trait and part of my research journey, I have chosen to leave the chapter unchanged.

The following section explores the origin of the incubator and its effect on neonatal care.

2.2 Evolution of the Incubator: From Fairground Attraction to the Mainstay of Modern Neonatal Intensive Care

There are various accounts of the development of the incubator. I retrieved the literature used to inform this section from various sources with the intention of providing a general overview of the origins of humidified incubator use. Published sources of information included books, original medical texts, individual comments and reflections, and secondary sources such as historical reviews that I had collected over time. In addition, I conducted a literature search using the following:

- databases: CINAHL, Medline, Old Medline, Embase and the Cochrane Database of Systematic Reviews
- search terms: infant/neonate/preterm/extreme prematurity, incubator/humidicrib/crib, humidity/humidification/humidified incubator,
This section in the chapter sets the scene and provides background to the use of humidified incubators, this historical context gives clarity to the challenges that neonatal clinicians face today. Further, the section describes the influence of individuals convinced of the rightness of their beliefs about the use of the incubator, political agendas of various governments and countries and the clinical practice environment on innovation, practice change and patient care—topics that I will return to later in the thesis.

The evolution of the preterm infant incubator is interesting and colourful. Although historians have traced the earliest incubator back to Johann Georg von Ruehl in Russia in 1835 (Raju 2006), a French obstetrician, Stéphane Tarnier, is credited with the introduction of incubators for preterm infants in 1880 (Budin 1907). There is also evidence of double-walled warming tanks invented by French paediatrician Denucé in 1857 (Cone 1981) and by Credé in Leipzig since at least 1864 (Credé 1884). Tarnier used a warm air incubator made of wood based on the design of a chicken incubator displayed in the Paris zoo (Budin 1907); the first version housed several preterm infants (known then as weaklings). Ventilation relied on simple convection and critics claimed that, by placing infants in a sealed box, Tarnier sacrificed ventilation to achieve thermoregulatory benefits (Credé 1884).

Undaunted by criticism and convinced incubators could improve infant mortality Tarnier persevered. Tarnier reported a case series comprised of more than 500 infants who were cared for in an incubator in which the survival of infants born between 1,200 and 2,000 grams increased from 38% to 66% (Auvard 1883). It is noteworthy that the case series included only the very small number of infants who were born in hospital (home birth was much more common) and probably included small for gestational age infants; however, Tarnier made no such distinctions. Of interest to this work is the fact that, although Tarnier did not mention the provision of humidity specifically, a short text about human incubators in *The British Medical Journal* (1897) described the passage of warm air through a wet sponge to create moisture. Clinicians used variants of this incubator for many years.
I have chosen to discuss the introduction of humidified incubators in two contrasting health care systems: in France, whose clinicians are accredited by history books with the invention and its early successes, and in the United States, where clinicians were late adopters of the innovation. I chose these countries because of their diversity; they highlight differences in belief systems and attitudes towards new technology and practice change as well as illustrating the influence of political agendas and societal responses on health care.

2.2.1 The incubator in France

More expensive and sophisticated incubators had been developed, but the maternity hospitals in Paris chose to use the modified version of Tarnier’s incubator. The incubator required a high degree of maintenance and constant attention. Although incubators were initially intentioned for the smallest and sickest infants in a ward, clinicians instead placed them beside the mothers’ beds. This initiative served two functions: the high-maintenance incubators did not affect nurse staffing levels because the mothers provided care for their infants and it promoted bonding (Klaus 1993) - something we still strive to achieve in NICUs today. The strategy worked well for some time in the Paris Maternity Hospital. In his account of this chapter in history, Baker (2000) postulated that the Paris hospital and the social environment of the time may have had a positive influence on the uptake of new technology. Before long, the primary focus of care was the preterm and sickly infants of the poor. Families perceived that infants placed in incubators would die and many of the poor abandoned their infants in the hospital.

In Nice, in 1891, Alexandre Lion developed a more sophisticated incubator (Smith 1896). Known as the Lion incubator, it was made of iron with glass front doors at eye level. Lion introduced ‘Baby Incubator Charities’, which made incubators available for those who needed it. The Lion incubator was expensive and designed to be used either for wealthy private patrons or by the poor, who in lieu of payment allowed their babies to be publicly exhibited; the fee charged to view them was used by Lion to fund the nurses and wet nurses who cared for them (Proctor 2004; Smith 1896). ‘Baby Incubator
Charities’ became popular attractions in Lyon, Marseilles, Nice and Paris during the 1890s. This contrasted significantly with the use of the Tarnier incubator in the Paris Maternity Hospital, which had become a symbol of lower socioeconomic families and infant abandonment.

High expectations of reducing infant mortality and implications for population growth attracted political attention. Years of falling birth rates and a declining population, which threatened to affect the number of potential future workers and military personnel, was causing significant anxiety. The French government viewed a potential decrease in infant mortality as a solution to the crisis and funded the manufacture, purchase and distribution of large numbers of incubators. However, the outcome of this intervention was not as expected.

Rapid and widespread introduction of the incubator into Paris maternity hospitals had catastrophic results. Mortality rates appeared to rise as increasing numbers of parents presented to hospitals with preterm infants, many of whom had been cared for at home and were near death on admission. This occurred because most preterm infants of that time died at home, often with birth and death unrecorded—a factor apparently not considered during the decision making and implementation of the innovation or in the evaluation of the intervention. Not surprisingly, political and medical interest in the preterm infant subsequently waned; no one wanted to be associated with an increased infant mortality rate. Preterm infants no longer received treatment and the concept of the incubator was almost abandoned for a period of 10 years (Baker 2000).

2.2.2 The incubator in the United States

While clinicians in France, Germany and later Great Britain used incubators, the treatment of preterm infants in the United States remained controversial. Preterm infant care was less of a social imperative as a rising eugenics movement questioned the value of the lives of preterm infants (Schneider 1982). Supporters of the movement considered preterm infants to be damaged individuals, especially because the incidence of prematurity was more prevalent among the underprivileged in society, and this fuelled mounting fear that increased survival of weaklings into adulthood could result in
offspring that were also weak and infirm. The *Buffalo Medical Journal* (1901, p. 56) reflected this opinion:

> [Medicine is] preserving the weakling, the deformed, and the tuberculous, and placing these defectives who would otherwise surely have perished in an active struggle for existence … in a condition to transmit their deficiencies, deformities and vices to generations as yet unborn. In its efforts to preserve the individual it [medicine] forgets to consider the effects of such action upon the race as a whole.

There was a simultaneous move from home to hospital birth and a focus on obstetric practices with a view to improving maternal care rather than preterm infant survival (Leavitt 1986). It is interesting to note that paediatricians had no access to maternity hospitals at that time.

As in France, decisions made about incubator purchase and implementation had unexpected consequences. When humidified incubators increased in popularity in the United States, the Lion incubator was the device of choice, perhaps because of a turn-of-the-century American enthusiasm for all things technical and automatic (Proctor 2004). The Lion incubators were costly; consequently, each maternity hospital purchased only a few and clinicians used them for the sickest infants, who often did not survive. Incubators quickly became associated with infant death and their use was abandoned (Proctor 2004).

Despite the poor outcomes and subsequent disrepute into which the incubator had fallen, supporters of infant incubators continued to seek alternative ways to increase awareness of what they believed to be their benefits. In 1901, Martin Couney, a physician-showman and entrepreneur born in Alsace, began displaying preterm infants in incubators at fairs, expositions and ‘freak shows’ around the world; these incubator baby shows became crowd-pulling exhibits that ignited international interest (Butterfield, Ballowitz & Desmond 1993; Silverman 1979). Demonstration of incubators containing live infants generated great optimism among both health professionals and the public. Such events also provided a rare opportunity for the transfer of knowledge and technology (Silverman 1979). Although he had many critics who questioned his motives, and we could describe his methods as unethical, unorthodox and bizarre, Couney’s zeal, persistence and dedication to the cause knew no bounds. He moved to the United States (Coney Island fairground was perhaps the most...
infamous) and continued to champion the incubator at fairs and shows until clinicians accepted it as a standard of care for preterm infants some 36 years later (Liebling 1939). Despite the apparent benefit of incubators on neonatal survival, it took a great many years to change clinician behaviour and encourage adoption of the new technology—a dilemma that researchers and clinicians still face today. Fairs and ‘freak shows’ as agents of change are an interesting concept.

Paediatricians finally assumed advocacy for preterm infants, and work continued in the intervening years to encourage acceptance of the incubator. Chicago obstetrician Joseph B. DeLee and paediatrician Julius Hess stressed the need for not only an incubator but also a supportive network to improve preterm infant care (Butterfield 1993; DeLee 1902; Hess 1934). Hess set about to test the hypothesis that a supportive network could improve infant outcomes. Following development of a new version of the incubator, both Hess and DeLee developed mobile transport systems to enable the safer transfer and treatment of out-born infants (Butterfield 1993; Hess 1915). Concurrently, Hess worked collaboratively with a head nurse to train a team of nurses to care for preterm infants using protocols (Butterfield 1993; Hess 1934). Responsible for the day-to-day running of the incubator station (nursery) and care of the infants, these neonatal nurses demonstrated an innovative nursing model for the early 1920s. Further, Hess published the first long-term follow-up studies of preterm infants to abate public and physician fear of creating future populations of impaired children and adults (Hess, Mohr & Bartelme 1934). Hess and his team cared for 9,022 preterm infants in incubators over a 30-year period, with a 73% survival rate (Hess 1953). Incubators soon became symbols of great promise—the quintessential icon of neonatal care—and, undoubtedly, made a great contribution to reducing neonatal mortality worldwide.

This comparison of the introduction of incubators in two countries is important to the work of the thesis. The review of the literature revealed two very different clinical, organisational and political contexts that influenced both the practice change and patient care in very different ways. Also evident were the challenges of and time taken to implement a new intervention and the influence of individuals in the process. The following section explores the evolution of incubator humidity and its role in improving preterm infant health outcomes.
2.3 The Incubator and Humidity

The evolutionary journey of humidification was equally as controversial as that of the infant incubator, and dispute about its use continues to the present day. In the 1930s, Blackfan and Yaglou (1933) reported improved outcomes for preterm infants nursed in warm, humidified environments. Seeking the ideal environment for preterm infants, the researchers studied the effects of varying atmospheric conditions on neonatal growth and development. This seven-year observational study comparing two time periods (pre and post intervention) found increased survival in a group of preterm infants weighing 1,360 to 2,270 grams at birth when nursed in an environment of 65% humidity compared with controls of similar birth weight in a lower ambient humidity of 30%. The preterm infant mortality rate was 96/229 (42%) in the post-intervention humidified environment compared with 64/123 (52%) in the pre-intervention, non-humidified group. The study design used open cots rather than incubators, and an air conditioning system humidified the entire nursery during the study period. While acknowledging the limitations of the retrospective design of the study, the researchers concluded that the findings did demonstrate benefit by increasing ambient humidity.

Over time, incubator manufacture and design continued to develop with increasing effectiveness. By the end of World War II, incubators were made of Lucite. Clinicians have used a version of these transparent boxes (cradles of glass) to manage sick and preterm infants since that time. The monitoring and titration of air temperature and humidity levels became possible with the design of more efficient heat sources and humidifying systems. By 1955, Smith (p. 2051) described the routine use of a relative humidity of 60% to 70% in the management of preterm infants. However, the literature of the time acknowledged that the level and duration of humidity required or tolerated by the preterm infant was unknown.

Seminal work by Silverman and colleagues (Silverman, Agate & Fertig 1963; Silverman & Blanc 1957; Silverman, Fertig & Berger 1958) in a series of well-planned RCTs in the 1950s and 1960s again demonstrated an association between the use of humidity, thermal stability and improved survival of preterm infants, stimulating
increased interest in humidity use. Sequential studies investigated the effects of various combinations of environmental temperatures and humidity levels on preterm infant mortality and morbidity. The first study in the series compared the effects of low-level (30–60%) versus high-level (80–90%) humidity on 324 preterm infants in incubators maintained at the same ambient temperature (28.9 °C, range 28.3 °C to 29.40 °C) (Silverman & Blanc 1957). The researchers reported a significant decrease in mortality within the first five days of life in infants receiving high-level humidity (RR 0.66, 95% CI 0.46, 0.94). However, there was no difference in overall mortality at 28 days. Further, the study found higher body temperatures in infants in the humidity group. The researchers postulated that raising body temperature and thus reducing the degree of hypothermia might be the key to reducing neonatal mortality.

To test the hypothesis that raising body temperature might reduce infant mortality, a second study compared the effects of two contrasting environmental temperatures (31.7 °C and 28.9 °C) on mortality and morbidity in 182 preterm infants when humidity levels were maintained between 80% and 90% (Silverman, Fertig & Berger 1958). Higher environmental temperatures were associated with improved survival rates, as the researchers had hypothesised. Silverman, Agate and Fertig (1963) designed the third and final study to determine the role of humidity in improving health outcomes for preterm infants. This study compared the effects of low-level (30–60%) versus high-level humidity (80–90%) on 352 infants (less than 1,500 grams at birth) maintained at the same body temperature (36.1 °C +/- 0.1 °C). Results revealed no statistically significant difference in mortality between the two groups on days 5 or 28. There was no statistically significant difference in short-term outcomes, including incidence of IVH, sepsis or weight loss in all three studies.

This work of Silverman and colleagues was pivotal to the accumulating evidence on the importance of thermal stability to preterm infant survival. Findings were consistent with other studies that described the relationship between increased body temperature and improved neonatal outcomes irrespective of the level of humidity (Buetow & Klein 1964; Day et al. 1964; Glass, Silverman & Sinclair 1968; Jolly, Molyneux & Newell 1962). Therefore, Silverman, Agate and Fertig (1963) came to the important conclusion that the role of humidity was not significant per se and that raising body temperature
(preventing hypothermia) was crucial to preterm infant survival. The researchers concluded that, since they had found no convincing evidence of any non-thermal benefits of humidification, humidity was not essential, and the provision of heat was sufficient.

Simultaneous reports that incubator humidity might contribute to nosocomial infection in neonatal nurseries further reduced its popularity. Published studies found organisms including *Pseudomonas, Candida* and *Legionella pneumophilia* within the nebulising units used to provide incubator humidity (Edmondson et al. 1966; Harpin & Rutter 1985; Hoffman & Finberg 1955; Reinartz et al. 1966; Sever 1959; Verissimo et al. 1990). Consequently, for several years clinicians cared for preterm infants in dry incubators that provided heat only.

In summary, early work in incubator humidity use attempted to reduce preterm infant mortality rates but fell out of favour when evidence pointed to the need for warmth rather than humidity. In addition, the incidence of nosocomial infection in the nebulising units that provided humidity gave cause for concern. However, a change in the gestational age of the infant population over time challenged the earlier decision not to humidify incubators. Increasing numbers of extremely preterm infants within NICUs provided the catalyst for this change. The second section of the chapter provides an overview of this shift in infant population and highlights the challenges of an immature epidermal barrier - challenges that brought about a resurgence of the use of incubator humidity in NICUs.

**2.4 Catalyst of Change: The Extremely Preterm Infant**

Improvements in a range of perinatal care practices have increased preterm infant survival, especially for infants born less than 28 weeks gestation (Cooke 2006; Darlow, Cust & Donoghue 2003; Doyle & the Victorian Infant Collaborative Study Group 2004; EXPRESS Group 2009; Field et al. 2008; Fischer et al. 2009; Hack 2006; Joseph et al. 2001; Stoelhorst et al. 2005; Wilson-Costello et al. 2005). However, morbidities have remained high, secondary to CLD, late-onset sepsis, severe IVH and NEC (Costeloe et al. 2000; Johnson et al. 2009; Stoll et al. 2010). It is significant that each of these
morbidity is an independent risk factor for poor neurodevelopmental outcomes. Increasing numbers of infants born at the cusp of viability (23–25 weeks) brought new challenges, new pathologies and new dilemmas with little evidence to guide clinical decision making. One major challenge and early priority was the management of heat and water balance - both the responsibility of the neonatal nurse.

Since the early work of Silverman, Fertig and Berger (1958) demonstrated that increasing body temperature through control of the thermal environment significantly reduced mortality in low birth weight infants, other investigators replicated the study with the result that thermal management became a cornerstone of the new field of neonatology (Brice, Rutter & Hull 1981; Buetow & Klein 1964; Glass, Silverman & Sinclair 1968; Hammarlund et al. 1977; Hey & Katz 1970; Pomerance & Madore 1974). In fact, the importance of body temperature as a predictor of outcome in preterm babies continues to be emphasised by its inclusion in risk scoring systems such as the Clinical Risk Index for Babies (CRIB) and the Score for Neonatal Acute Physiology—Perinatal extension (SNAPPE-II) (Parry, Tucker & Tarnow-Mordi 2003; Richardson et al. 2001). Hypothermia on admission to the NICU remains an independent predictor of neonatal mortality and morbidity (Costeloe et al. 2000; Oxley & Lyon 2001; Parry, Tucker & Tarnow-Mordi 2003).

Temperature control, therefore, is essential to survival. The aim of thermal management is to provide a thermo-neutral environment that maintains the infant’s body temperature within normal range without increasing either oxygen consumption or metabolic rate. Humans can maintain an almost constant body temperature (36.5 °C to 37.5 °C) in a wide range of thermal environments. Hypothermia in infants has been defined by the World Health Organization and classifies a core body temperature of 36 °C to 36.4 °C as mild hypothermia, 32 °C to 35.9 °C as moderate and less than 32 °C as severe (World Health Organization 1997). Currently, however, there is no accepted formal definition of a ‘normal’ temperature for preterm infants. Extremely preterm infants present a thermal challenge for clinicians, who struggled to achieve and maintain an optimal microenvironment for extremely preterm infants even with the advent of modern incubators; simply providing heat did little to raise body temperature in the most immature infants.
Understanding the basic physiological principles and specific challenges facing extremely preterm infants in relation to thermoregulation and fluid balance helps explain the decision-making processes that subsequently led to practice change. The following pages explore the consequences of immature skin after birth.

2.4.1 Consequences of an immature epidermal barrier

The skin is a vital organ necessary for survival outside the aqueous uterine environment. As with other epithelial surfaces (lung, gut and kidney) that interface with the environment after birth, the skin must immediately perform multiple vital functions. The most important function of the skin is to act as a barrier, preventing dehydration from the loss of body water, hypothermia from heat loss, poisoning from the absorption of drugs and chemicals, and systemic infection from invading microorganisms, as well as protection against physical trauma (Harpin & Rutter 1983). The major barrier lies within the most superficial and outer layer of the epidermis: the stratum corneum. Although keratinisation begins around 18 weeks gestation, the epidermis is still very thin, barely visible, poorly formed and functionally weak at 26 weeks gestation (Evans & Rutter 1986a; Rutter 1988). The stratum corneum may be only one to two cell layers thick or even absent in the most preterm infants (Rutter 1987). Visually, the skin appears red, gelatinous and transparent, and the blood vessels that lie beneath are clear.

Not surprisingly, extremely preterm infants suffer from a myriad of structural and functional deficits because of this immature epidermal barrier that have important clinical consequences (Cartlidge 2000; Rutter 2000b). Thin, functionally immature skin in combination with a large surface area to body mass ratio, little or no subcutaneous fat, decreased glycogen stores and high body water content predisposes extremely preterm infants to evaporative heat and water loss (Lyon et al. 1997). Although a temporary problem while the immature infant adjusts to life in a gaseous environment, failure to achieve and maintain thermal stability and an adequate fluid and electrolyte balance in the early neonatal period caused by excessive evaporative losses is associated with significant morbidity. Reported complications of high evaporative losses include hypothermia, weight loss, hypernatraemic dehydration, hyperkalaemia, impaired renal
function, metabolic acidosis, hypovolaemia and IVH (Costarino et al. 1992; Kaplan, Siegler & Schmunk 1998; Omar et al. 2000; Rutter 2003; Thomas 1976). This evaporative loss through the skin, known as transepidermal water loss (TEWL), is the major cause of heat loss in extremely preterm infants in the first few weeks of life.

TEWL is one of the most important biophysical parameters for evaluating epidermal barrier function. Water diffuses outward through the skin in a continuous passive process that is not subject to homeostatic control. During evaporation, water converts from a liquid to a gas. As the water vapour escapes into the air because of a vapour pressure gradient between the body surface and the air, heat is also lost from the infant into the air. The evaporative rate is proportional to the water vapour pressure gradient between the skin and the environment, and is independent of the temperature gradient between the skin and the environment. While high levels of TEWL reflect epidermal barrier immaturity or impairment (Nilsson 1977), TEWL also depends on environmental factors such as atmospheric (room) temperature and humidity as well as the humidity and airspeed within the incubator (Belghazi et al. 2005). Consequently, it is not possible to predict an individual infant’s fluid requirements; serum sodium levels and weight loss or gain provide an estimation of fluid requirements.

Researchers have reported the use of various approaches and instruments to measure the evaporation rate of water from the skin. The most commonly used hygrometry system consists of an open chamber diffusion technique using an instrument such as an Evaporimeter™ or Tewameter™ that measures water vapour pressure in g/m²/h according to Fick’s law (Barel & Clarys 1995). The water vapour pressure measurement provides an estimation of TEWL (Ariagno et al. 1997; Sedin et al. 1985). Using such instruments, researchers have demonstrated that evaporative losses are inversely related to gestational age; TEWL is most pronounced in the most immature infants in the first few days after birth and decreases with increasing postnatal and gestational age (Agren, Sjors & Sedin 1998; Hammarlund & Sedin 1979a, 1982; Hammarlund, Sedin & Stromberg 1983; Hammarlund, Stromberg & Sedin 1986; Harpin & Rutter 1985; Kalia et al. 1998; Maurer et al. 1984; Nonato et al. 2000; Rutter & Hull 1979; Wilson & Maibach 1980). Hammarlund and Sedin (1979a) observed that infants born at 25 weeks gestation lost 15 times more water than term infants at birth. Similarly, other studies
have reported TEWL exceeding 100g/m²/h (in excess of 200 mL/kg/day) in infants at the limit of viability (Rutter 2003; Schaffer & Weisman 1992). For every millilitre of water that evaporates from the extremely preterm skin, 560 calories of heat are lost (Rutter 2000a).

Routine care practices further contribute to TEWL. Paramount, therefore, is an understanding of the effect of routine interventions and commonly used therapies in the management of extremely preterm infants before complete epidermal barrier function is established. Invasive procedures necessary for both investigative and therapeutic purposes cause trauma; topical antiseptics and removal of tape and adhesive causes epidermal stripping, skin breakdown and abrasions predisposing to pain and increased permeability of the already ineffective barrier, which increases not only TEWL but also sepsis risk (Harpin & Rutter 1983; Lund et al. 1997; Okah et al. 1995). The use of overhead radiant warmers (Flenady & Woodgate 2009) and phototherapy (Grunhagen et al. 2002; Maayan-Metzger et al. 2001; Oh & Karechi 1972; Wu & Moosa 1978) increases TEWL and fluid requirements (Meyer et al. 2001).

Evidence has yet to emerge in relation to the timing of achievement of complete barrier function in extremely preterm infants. Rapid skin maturation is evident in both human and animal models following exposure to air (Denda et al. 1998; Evans & Rutter 1986a; Hanley et al. 1997; Prunieras, Regnier & Woodley 1983), and TEWL significantly reduces over the first week of life (Agren, Sjors & Sedin 1998; Agren, Sjors & Sedin 2006; Hammarlund, Stromberg & Sedin 1986; Harpin & Rutter 1983; Kalia et al. 1998; Rutter & Hull 1979). Nonetheless, extremely preterm infants exhibit continued compromise of the epidermal barrier for several weeks after birth. In a sample of 101 term and preterm infants of varying gestational ages and birth weight, Hammarlund, Sedin and Stromberg (1983) found the level of TEWL to be twice as high as that of term infants at four weeks of age. Functional studies of the skin of extremely preterm infants reported a lack of maturity until two to four weeks postnatal age irrespective of gestational age at birth (Evans & Rutter 1986a; Hammarlund, Sedin & Stromberg 1982a; Harpin & Rutter 1983). However, the studies have limited generalisability because the study samples did not include extremely preterm infants.
Further studies report similar findings; in addition, they provide information that high levels of TEWL may persist beyond two to four weeks of life in the most immature infants. A Swedish study measured the rate of evaporation of water from the skin of 24 and 25 week gestation infants and found that, at 28 days of life, TEWL remained twice as high as previously reported in slightly more mature infants born at 25 to 27 weeks gestation and four times as high as that reported in term infants (Agren, Sjors & Sedin 1998). Similarly, a longitudinal study conducted by Kalia and colleagues (1998) in the United States reported that the stratum corneum may not achieve functional and structural integrity until five to seven weeks postnatal age in infants less than 25 weeks gestation. The researchers concluded that 30 weeks postmenstrual age might be an important milestone in skin maturation, irrespective of gestational or postnatal age. The results of these studies imply that barrier function may develop at a much slower rate than the rapid structural epidermal maturation observed in the early days and weeks after birth. However, this study included only 10 infants whose gestational age at birth was 23 to 25 weeks.

Attempts to accelerate epidermal barrier maturation in the postnatal period have been unsuccessful. Various approaches have attempted to reduce evaporative losses, protect the immature skin and increase barrier function in clinical practice. Methods used include waterproof coverings such as bubble wrap or cling film (Marks, Friedman & Maisels 1977); semipermeable membranes such as plastic dressings, blankets and bags (Baumgart 1984; Besch et al. 1971; Bredemeyer, Reid & Wallace 2005; Evans & Rutter 1986b; Mancini et al. 1994; Vernon et al. 1990; Vohra et al. 1999; Vohra et al. 2004); and exogenous topical agents, primarily emollient ointments (Brice, Rutter & Hull 1981; Lane & Drost 1993; Nangia et al. 2008; Nopper et al. 1996; Rutter & Hull 1981). Research suggests that these measures reduce TEWL and improve skin integrity (Mancini et al. 1994; Nopper et al. 1996); however, reported widespread use belies the paucity of knowledge regarding the mechanisms of action and potential associated risks. In fact, a Cochrane systematic review of four RCTs found an increased risk of nosocomial sepsis attributed to ointment used to protect the epidermal barrier (Conner, Soll & Edwards 2003). The review found extremely preterm infants treated with prophylactic topical ointment to be at increased risk of coagulase negative staphylococcal infection (RR 1.31, 95% CI 1.02, 1.70) and any nosocomial infection
(RR 1.20, 95% CI 1.00, 1.43). The review concluded that clinicians should not use ointments on the skin of extremely preterm infants.

Although the literature primarily attributes TEWL to the structural properties of the epidermis, research has offered additional possibilities. One example is the influence of the mechanisms that facilitate water transport. Aquaporin (AQP) water channels distributed throughout different tissues allow rapid and regulated transcellular water transport. Agren and colleagues (2003) found increased AQP in fetal and preterm rat pups and postulated that this may influence skin hydration and water transport, contributing to the high water loss through immature skin. This work was the subject of Johann Agren’s PhD, and further research in this area continues by the research team in Uppsala University, Sweden. The work adds support to previous studies proposing that transepidermal water movement may play an important role in epidermal homeostasis and development (Grubauer, Elias & Feingold 1989; Proksch et al. 1993; Prunieras, Regnier & Woodley 1983).

An antenatal intervention may also reduce postnatal evaporative losses. Some work suggests that antenatal corticosteroids given to mature fetal lungs prior to preterm birth may enhance epithelial cell maturation, improve skin barrier function and reduce insensible water losses (Dimitriou et al. 2005; Omar et al. 1999). However, a study of barrier maturation in preterm infants demonstrated no epidermal effect following the administration of antenatal steroids (Jain, Rutter & Cartlidge 2000). Similarly, Dollberg and colleagues (2000) found no difference in the thermal capabilities in infants less than 1,000 grams at birth who were treated with antenatal steroids compared with infants who were not.

In the future, it may be possible to stimulate normal development of skin barrier function (either in utero, if possible, or in the postnatal period) and/or provide a physiologic temporary artificial barrier. Studies of fetal rat barrier development suggest that acceleration of this process is possible (Hanley et al. 1999; Williams et al. 1998), but these findings have not yet been replicated in humans. Until normal barrier function can be stimulated or a safe artificial barrier provided, reducing evaporative losses and
maintaining skin integrity will continue to prove challenging in the management of the most immature infants.

In summary, extremely preterm infant physiology places the infant at risk of heat and fluid imbalance, which can have life-threatening consequences. Transepidermal water and heat loss are highest immediately after birth and reduce with increasing postnatal age; the highest losses are evident in the most preterm infants, placing them at greatest risk. Attempts to alter or protect the epidermal barrier to reduce TEWL have been largely unsuccessful, so methods to achieve and maintain an adequate fluid balance are essential to optimise outcomes.

The next part of this second section highlights the challenge of achieving and maintaining an adequate fluid and electrolyte balance in extremely preterm infants with high evaporative losses.

2.4.2 Fluid and electrolyte balance

There is agreement in the literature that achievement and maintenance of an adequate fluid and electrolyte balance in extremely preterm infants is one of the greatest challenges in neonatology. The main determinants of fluid management rely on knowledge of the processes of neonatal adaptation; an estimation of TEWL; an awareness of glomerular filtration rate and how this can be influenced by age, respiratory distress and medical intervention; and an understanding of tubular function and its maturation (Hartnoll 2003). The fine balance between dehydration and fluid overload can be difficult to achieve, the margin for error extremely small and the consequences significant.

Fluid balance in the extremely preterm infant is challenging for many reasons. Mobilisation and excretion of the extracellular fluid excess is a prerequisite for successful postnatal adaptation (Shaffer & Meade 1989). There is a redistribution of water from the interstitial space to the extracellular space and simultaneous reabsorption of lung fluid. Sodium is the principle electrolyte of extracellular fluid, and an obligatory sodium loss with a subsequent negative sodium balance reflects the expansion of the
extracellular water (ECW) volume and is unrelated to the volume of fluid administered (Tang, Ridout & Modi 1997). Early contraction of the ECW compartment occurs because of the loss of interstitial fluid (Bétrémieux et al. 1995; Modi & Hutton 1990) and is characterised by a diuresis and postnatal weight loss. The timing of the contraction of the extracellular compartment is interrelated with cardiopulmonary adaptation; respiratory function improves following diuresis. Once the ECW compartment stabilises, the newborn infant’s ability to maintain fluid and electrolyte homeostasis improves.

As with most physiological processes, the likelihood and magnitude of perturbations in fluid and electrolyte status correlate with the degree of prematurity and associated conditions. The body composition of the extremely preterm infant is predominantly water (80–90%) (Hartnoll, Betremieux & Modi 2000; Tang, Ridout & Modi 1997) and there is proportionally more fluid in the ECW compartment than the intracellular compartment compared with term infants. Consequently, the more preterm the infant the more pronounced the contraction of the ECW space and the higher the insensible water loss. There is additional and substantial water loss from the intracellular compartment secondary to high osmotic pressure in the extracellular space and high TEWL. Rapid loss of free water provides a hyperosmolar extracellular compartment characterised by hypernatraemia, often complicated by hyperglycaemia, and an accompanying shift of potassium that causes potentially life-threatening hyperkalaemia (Omar et al. 2000). Respiratory distress syndrome, mechanical ventilation and exogenous sodium administration delay contraction of the ECW compartment and the onset of diuresis further complicating the clinical course (Modi & Hutton 1990).

Further compounding the issues of fluid balance in the extremely preterm infant is an immature renal system. Urine output is low in the first few days after birth and is independent of fluid intake. The combination of immature nephrons and a low glomerular filtration rate (Aperia et al. 1981; Gallini et al. 2000; Sonntag, Prankel & Waltz 1996; Vanpee et al. 1993) contributes significantly to the preterm infant’s limited ability to compensate for varying water and solute loads by adjusting the concentration of urine (Schaffer & Weisman 1992). In particular, the ability to both retain and excrete sodium is limited because of impaired reabsorption at the proximal tubule, limited
aldosterone responsiveness at the distal tubule, limited intestinal absorption and an immature sodium/potassium pump mechanism (Al-Dahhan, Haycock & Nichol 1984; Haycock & Aperia 1991). Mechanical ventilation (Coulthard & Hey 1999) and a clinically significant PDA (Bomelburg & Jorch 1989; Vanpee et al. 1993) further compromise the glomerular filtration rate.

Despite being the focus of neonatal research for many years, some controversy still surrounds optimal fluid requirements and the role of fluid balance in adverse health outcomes for extremely preterm infants. Existing evidence suggests that fluid balance in the first days to weeks of life is an important factor influencing neonatal morbidity (Bell & Acarregui 2008; Bell et al. 1980; Modi 2004). Nevertheless, no precise guidelines to optimise fluid therapy in extremely preterm infants exist. Much of the published work does not reach consensus and, in general, is conflicting, confusing and difficult to interpret because studies use various definitions, fluid regimes and outcome measures. Controversy centres primarily on varying opinions about the benefits and risks of liberal versus restricted fluid regimens.

Several studies have investigated the effect of the administration of varying fluid volumes on neonatal outcomes. Retrospective and observational studies report an increased risk of patent ductus arteriosus (PDA) (Bell et al. 1980; Evans 1993; Rojas et al. 1995; Stephens et al. 2008; Stephens et al. 2005; Stevenson 1977), CLD (Bell 1992; Brown 1979; Brown et al. 1978; Marshall et al. 1999; Palta et al. 1991; Tammela & Koivisto 1992; Van Marter et al. 1990; Wadhawan et al. 2007) and mortality (Stephens et al. 2008; Tooley 1979) with liberal fluid use. Equally, some observational studies have shown no difference in the early fluid regimens (first four to 14 days) of infants who develop CLD (Niwas, Baumgart & DeCristofaro 2010; Spahr et al. 1980) or PDA (Furzan et al. 1985; Mouzinho, Rosenfeld & Risser 1991; Niwas, Baumgart & DeCristofaro 2010) compared with those who do not.

Proponents of a fluid restricted strategy allow for a negative water balance in extremely preterm infants in the first few days of life. However, a prerequisite for fluid restrictive management is the provision of a means to reduce evaporative losses, such as supplemental humidity. The rationale for proposing a fluid restrictive strategy is that the
administration of high fluid volumes to avoid dehydration and replace expected water and sodium losses could cause volume overload. The resultant positive water and sodium balance and expansion of the extracellular space have been associated with increased morbidity (Modi 2004). The negative effects of a positive water balance was demonstrated by Oh and colleagues (2005), who summarised fluid balance data from more than 1,300 extremely low birth weight infants (birth weights 401–1,000 g). Regression analysis showed lower birth weight, higher fluid volumes and absence of weight loss in the first 10 days of life were significantly associated with a higher risk for death and CLD (composite outcome).

Fluid restrictive strategies may increase the risk of hypernatraemic dehydration and compromise nutrition and growth. Hypernatraemic dehydration—a potentially lethal condition—occurs because of inadequate fluid administration, excessive fluid loss or excessive sodium intake. Described complications of hypernatraemic dehydration include hypovolaemia, hyperosmolarity, hyperkalaemia, cardiac arrhythmia, renal failure, severe hyperbilirubinaemia, cerebral oedema, intracranial haemorrhage, hydrocephalus, thrombosis and death (Costarino et al. 1992; Kaplan, Siegler & Schmunk 1998; Laing & Wong 2002; Lupton et al. 1990). In fact, in one small study, Coulthard and Hey (1985) demonstrated the safe administration of fluid volumes up to 200mL/kg/day in 39 term and preterm infants. However, the study sample included only healthy infants who were greater than or equal to 27 weeks gestation. Further, animal work by Agren and colleagues (2003) found that a restriction in fluid and energy intake led to high TEWL and skin water content during the first postnatal days in rat pups.

To date, only five prospective RCTs have assessed the risks of high versus low fluid intake in very low birth weight infants (Bell et al. 1980; Kavvadia, Greenough & Dimitriou 2000; Lorenz et al. 1982; Tammela & Koivisto 1992; von Stockhausen & Strive 1980). An updated Cochrane review summarised the trials (Bell & Acarregui 2008). The review revealed what appeared to be significant advantages to a fluid restrictive strategy in the management of preterm infants. When considered collectively in a meta-analysis of four trials (Bell et al. 1980; Kavvadia, Greenough & Dimitriou 2000; Lorenz et al. 1982; Tammela & Koivisto 1992), the infants who were in the fluid restricted groups were at a significantly lower risk of PDA (RR 0.52, 95% CI 0.37,
Based on this analysis, the number needed to treat with restricted water intake to prevent one case of PDA was seven (95% CI 5, 14). The risk of NEC was also reported to be significantly lower with restricted water intake (RR 0.43, 95% CI 0.21, 0.87); the number needed to prevent one case of NEC was 20 (95% CI 11, 100). Not surprisingly, postnatal weight loss (expressed as a percentage of birth weight) was significantly higher with restricted water intake in the meta-analysis of three trials (Bell et al. 1980; Tammela & Koivisto 1992; von Stockhausen & Strive 1980). There was a reported trend toward increased risk of dehydration and reduced risks of CLD, IVH and death with restricted fluid intake but these trends were not statistically significant. Of note, study protocols differed in the timing and duration of fluid regimens and there was underrepresentation of extremely preterm infants in all trials, so clinicians must interpret the findings of the review with caution.

In summary, a prerequisite for thermal stability and adequate fluid balance is the provision of a means to replace or reduce evaporative losses. Based on evidence to date, it seems prudent that the prescription for fluid intake should be one of careful restriction, to reduce rather than replace evaporative losses. This sparked renewed interest in the humidified incubator.

The third section of this chapter provides an overview of the role of ambient humidity in water and heat balance and explains why the humidified incubator regained popularity following the admission of increasing numbers of extremely preterm infants to NICUs. This section also seeks to determine evidence to inform practice and identify potential benefits and risks of humidification. Finally, the chapter summary brings all aspects of the chapter together to examine contemporary issues and questions about humidification of incubators, reflect on my learning and consider the implications of the findings on the proposed study.

### 2.5 Incubator Humidity: The Evidence

Humidity, most commonly expressed as relative humidity (% RH), is the amount of water vapour contained in the air at a particular temperature compared with the total amount of water vapour the air can contain at that temperature. The capacity of air to
hold water vapour varies according to the temperature of the air. The warmer the air the more water vapour it can hold; as air cools its capacity to hold water decreases. However, although raising the temperature increases the capacity of air to hold water, water is not always available to move into the air to fill that increased capacity. Therefore, changes in temperature often lead to quite significant alterations in the relative humidity. For example, in a sealed box such as an incubator containing a fixed amount of water vapour, raising the temperature will decrease the relative humidity (Harpin & Rutter 1985). This is because the capacity of the air to contain water has increased but the actual amount of water has remained the same. Heat in the presence of low humidity increases skin permeability and surface evaporation, increasing the potential for evaporative heat and water loss. Put simply, infants in incubators with high air temperatures have higher levels of TEWL because the air can hold no more water; the warm skin promotes additional fluid and heat loss, thereby decreasing core body temperature. This explains why infants remain hypothermic despite the use of very high incubator temperatures in the absence of supplemental humidity. Rutter (2000a) described this phenomenon as the ‘refrigerating incubator’. To understand why increasing the humidity within a microenvironment reduces TEWL, the work of this thesis now considers observational and physiologic work.

Since the early work of Silverman and Blanc (1957), several studies have examined the effect of humidity on short-term health outcomes, including TEWL, body temperature, fluid and electrolyte balance, skin integrity, PDA, CLD and sepsis. Small physiological studies have investigated the relationship between TEWL and ambient relative humidity (Hammarlund et al. 1977; Hammarlund & Sedin 1979b; Hammarlund & Sedin 1980, 1982; Hammarlund, Sedin & Stromberg 1982a; Hammarlund, Sedin & Stromberg 1983; Hammarlund, Stromberg & Sedin 1986; Harpin & Rutter 1985; Miller et al. 1961). Results indicated that the relationship is an inversely linear one; TEWL reduces with increasing humidity and ceases when relative humidity reaches 100% (Sedin, Hammarlund & Stromberg 1983). TEWL is zero in 100% humidity because there is no water vapour pressure gradient driving water loss, regardless of the effectiveness of the epidermal barrier. The studies recommended that the preterm infant be nursed in high-level humidity for the first few days or weeks of life while TEWL is at its highest level. However, the provision of 100% humidity, if appropriate, can be difficult to achieve.
and maintain in the clinical setting, and use of lower levels of humidity is more common. Some evidence suggests that 80% to 90% humidity reduces evaporative losses to a minimum. Takahashi, Hoshi and Nishida (1994) demonstrated a reduction in water loss to less than 40 mL/kg/day in infants less than 1,000 grams with the introduction of 90% ambient humidity. The researchers postulated that reducing evaporative losses would reduce fluid requirements and morbidities associated with administration of high fluid volumes.

Harpin and Rutter (1985) reported the effect of high-level humidity (80–90%) versus no humidity in 62 infants less than 30 weeks gestation. The study compared 33 infants exposed to high-level humidity for a two-week period with a retrospective cohort of 29 infants who received no supplemental humidity. Outcome measures included TEWL, body temperature and sepsis. The study found that the provision of high-level humidity reduced TEWL without delaying barrier maturation, improved thermal stability and increased incidence of *Pseudomonas* colonisation. Seventeen infants (57%) were colonised with *Pseudomonas* species during their hospital stay compared with six infants (21%) in the non-humidity group (p < 0.05). There was no significant difference in incidence of culture positive sepsis. The researchers concluded that supplemental humidity should be provided in the first few days of life only (when TEWL is at its highest level) to reduce sepsis risk. The study also reported an increased incidence of hyperthermia in infants in the humidity group and, although the methodology used did not permit direct comparisons, the researchers reported delayed ductal closure in infants within this group. The fact that fluid intake remained unchanged during the study period might explain the delay in ductal closure. High-level humidity in combination with the administration of large fluid volumes may have contributed to the increased incidence of PDA observed. The small sample size and number of extremely preterm infants and the retrospective nature of this study make conclusions difficult to generalise to the wider neonatal population.

Berry, Dougherty and Usher (1996) reported results from a retrospective study comparing humidity versus no humidity following a practice change from open beds to humidified incubators in infants weighing less than 1,000 grams at birth. The study compared 31 infants who received 70% to 80% humidity with 60 infants who received
no humidity. Infants in non-humidified incubators had higher mean serum sodium at 152.9 (SD 4.9) versus 143.5 (SD 9.4) mEq/L (p < 0.001) for infants who received humidity. After excluding infants without umbilical lines, 2/16 infants in the humidity group and 33/55 infants in the non-humidified group had maximum serum potassium measurements of greater than 6.9 mEq/L (p = 0.04). These differences occurred despite reduction in fluid administration (p < 0.02 all days to day 21 of life). The researchers concluded that the infants who received humidity had better early hydration and decreased fluid requirements. Again, the retrospective nature of this single-centre study makes conclusions difficult to generalise to the wider neonatal population.

A team at Ohmeda Medical (Locke et al. 2000) reported findings from a small, non-randomised study determining the effect of increasing incubator humidity during the first two weeks on serum sodium levels, skin integrity and sepsis rates. Thirteen infants received humidification (45–60%) while 23 infants received standard care (no supplemental humidity). Groups were comparable for birth weight and illness severity. Results suggested that infants in the humidity group had improved skin integrity (p < 0.04) and serum sodium levels (p < 0.05) and no difference in rates of proven or suspected sepsis (p = 0.05). However, the lack of randomisation and insufficient power made definitive conclusions difficult.

In a retrospective comparison, Gaylord and colleagues (2001) compared the effect of humidity (mean 64% RH) versus no humidity on the fluid and electrolyte management of 155 infants less than 1,000 grams at birth. The study measured outcomes pre and post introduction of humidity as a standard of care. The main outcomes included total daily fluid requirement, weight, urine output, serum electrolytes and incidence of PDA, CLD and sepsis. Infants in the non-humidified group had higher daily fluid requirements (p = 0.017) and lower urinary output (p = 0.043) in the first three days of life compared with those in the humidified group. The researchers also found a significant increase in incidence of hypernatraemia, hyperkalaemia and azotaemia in infants in the non-humidified group. There was no difference in incidence of PDA, CLD or weight at discharge. Although there was no increase in incidence of culture positive sepsis or typical waterborne pathogens, there was a statistically significant increase in colonisation of gram-negative organisms (Escherichia coli and Klebsiella pneumonia)
The researchers speculated that the increase in gram-negative isolates was the result of coincident changes in obstetric management in Group B streptococcal chemoprophylaxis and a concurrent nationwide shortage of penicillin that led to the use of broad-spectrum antibiotics. Again, the retrospective nature of this study and the issues of comparing two separate times makes generalisation of results problematic.

In contrast to the findings from the previously mentioned studies, the interim analysis of a prospective RCT ($n = 34$) that compared high-level humidity (80–85%) with standard humidity (50–55%) found no difference in fluid requirements, weight loss or incidence of PDA or sepsis in infants less than 1,000 grams at birth (Sapiegiene et al. 2004). Although this trial did include extremely preterm infants, the fact that the study was never completed (because of clinician attrition) in combination with a failure to reach the target sample size ($n = 60$) limits the reliability of results.

### 2.5.1 Potential risks of humidity use

The literature identified three risks associated with incubator humidity use. The first of these is a longstanding concern that humidified environments increase sepsis risk. The warm, moist conditions created within the humidified incubator are intrinsically ideal for bacterial and fungal growth. Condensation or rainout—a frequent complication of high humidity—reduces visibility and results in damp skin and bedding adding further concern (Rutter 2003). Although studies of early humidifying systems reported the presence of organisms (Chao, Hsieh & Hwang 1989; Hoffman & Finberg 1955; Rutter & Hull 1979; Sever 1959; Verissimo et al. 1990), recent modifications to humidifiers and the change in neonatal practices over time suggest that relating previous findings to modern-day practices may be inappropriate. Whether incubator humidity contributes to current sepsis rates is unknown.

Reducing the risk of sepsis in this infant population is paramount. Sepsis is now the major contributing factor to morbidity and mortality in extremely preterm infants (Adams-Chapman & Stoll 2006; Kaufman & Fairchild 2004; Pessoa-Silva et al. 2001; Stoll et al. 2002; Stoll et al. 2004; Stoll et al. 2010). During their hospital stay, 20% to
58% of extremely preterm infants experience a serious systemic infection (Isaacs et al. 1996; Kaufman & Fairchild 2004; Rubin et al. 2002; Stoll et al. 2004; Stoll et al. 2010; Van der Zwet, Kaiser & Van Elburg 2005; Zafar et al. 2001). Mortality is as much as three times higher for infants who develop sepsis compared with those who do not (Stoll et al. 2002) and accounts for approximately 50% of all deaths beyond the second week of life (Stoll & Hansen 2003). Complications associated with sepsis include CLD, PDA and NEC (Stoll et al. 2010). In addition, the literature describes poor growth and long-term neurodevelopmental sequelae including cerebral palsy (CP) and periventricular leukomalacia (PVL) in survivors (Petersen et al. 2006; Stoll et al. 2004).

The second risk of humidity use is hyperthermia (body temperature greater than 37.5 °C). Given the importance of thermal stability in the management of preterm infants, body temperature is the most frequently studied outcome measure of humidity use. Several studies reported increased body temperatures and a reduced incidence of hypothermia because of increasing the level of incubator humidity (Belgaumkar & Scott 1975; Hammarlund et al. 1977; Hammarlund, Stromberg & Sedin 1986; Hanssler & Breukmann 1993; Harpin & Rutter 1985; Hey & Katz 1970; Hey & Maurice 1968; Silverman, Agate & Fertig 1963; Silverman & Blanc 1957; Sulyok, Jaquier & Prod'hom 1973; Sulyok, Jequier & Ryser 1972). However, in avoiding hypothermia, there is always the risk of causing iatrogenic hyperthermia because the inability of the extremely preterm infant to disperse heat leads to vasodilation, tachycardia, lethargy and apnoea (Malin & Baumgart 1987; Tirosh et al. 1998). Longer term consequences of hyperthermia of extremely preterm infants are unknown, but some evidence has suggested they are less able to tolerate temperatures at the upper end of the normal range (Simbruner et al. 2005). Therefore, close monitoring to prevent iatrogenic hyperthermia may be as important as the prevention of hypothermia.

The literature identifies delayed epidermal barrier development as the third potential risk of humidity use. Results from a small prospective RCT involving 22 extremely preterm infants indicated that the level of humidity provided influenced skin barrier development (Agren, Sjors & Sedin 2006). The provision of moderate levels of humidity (70%) when compared with low-level humidity (50%) at 14 days of age and beyond delayed epidermal maturation resulted in persistently high levels of TEWL.
This finding confounded the belief that high humidity always reduces TEWL but did support theories that transepidermal water movement may be one of the driving forces behind the maturation process and that xeric stress is one of the foremost stimulators of skin keratinisation (Agren et al. 2003; Denda et al. 1998; Grubauer, Elias & Feingold 1989; Hanley et al. 1997; Prunieras, Regnier & Woodley 1983). The study suggested that the level of humidity over time might be an important factor to consider when providing an optimal environment for extremely preterm infants. Further research involving a larger numbers of infants would be useful to confirm this potentially important finding. The study reported no differences in body temperature, fluid requirements, serum sodium levels or weight loss between the two study groups.

### 2.6 Reflections, Learning and Critical Questions

I was initially pleased that the chapter did confirm my suspicion that optimal levels and duration of humidity had not been determined and there was virtually no robust evidence of the effect of humidification on clinically important neonatal health outcomes. However, my excitement was not to last. The available literature about incubator humidity was broad, somewhat vague and of limited use to direct clinical care, so it was of limited use in study design. This reality left me with more questions than it had answered and had implications for the proposed study that I had not anticipated. The absence of clear evidence complicated decisions about what the study might look like.

What specific research questions should I ask? Which outcome variables should I include? Which of the potential outcome variables should be primary and which should be secondary outcome variables? How do I determine this? Is there another way to examine the evidence?

### 2.7 Chapter Summary

This chapter presented the evolution of the humidified incubator and the arguments for and against its use over time, thus providing context for the work of the thesis. Adequate fluid and electrolyte balance is essential for extremely preterm infant survival.
Physiological studies tend to favour the use of incubator humidity, suggesting it is an important element in controlling evaporative heat and water loss, thus promoting physiologic stability. However, although humidification of the incubator has biological plausibility for reducing TEWL in extremely preterm infants, optimal levels and duration of humidity have not been determined for infants of varying gestational ages and the effect of use on clinically important outcomes is largely unknown. Further, the literature identifies potential risks of humidity use. The major concern is the potential for nosocomial sepsis in warm, moist humidified environments; other identified risks of humidity are hyperthermia and delayed barrier maturation. The lack of good quality research to inform practice creates uncertainty and challenges neonatal clinicians who direct care. Since this population of infants is at high risk of later developmental sequelae and the aetiology of many disabilities remains uncertain, it is vital that we make the right treatment choices. Improving our understanding of interventions that aid stabilisation following birth, such as incubator humidity, might influence long-term health outcomes. More research is required.

Further, the evolution of the humidified incubator is not only an interesting tale; it has specific relevance to neonatal care today. The history of the humidified incubator paints a picture that reflects the complexities of the health care world, the effects of the social, political and clinical context, the roles and attitudes of the characters involved and how together this influences both the practice environment and patient care. This historical account epitomises, for multiple reasons, the challenges of innovation and practice change that clinicians face on a daily basis in the current health care climate.

Contemporary thinking focuses on the systematic review of RCTs to assess the efficacy of clinical interventions. Therefore, I hoped that using the criteria and methods considered the gold standard might be a better way to provide insight into the evidence for humidification practices and provide guidance on which outcome variables would be the most appropriate for a future RCT of incubator humidity. In the following chapter, I present the systematic review that I undertook to critically appraise and determine the level of evidence for incubator humidity use in the management of preterm infants.
Chapter 3: C’ing the Very Small Body of Facts: 
Research Evidence in Context

A Systematic Review of Randomised Controlled Trials of Incubator Humidity

3.1 Chapter Overview

Having explored the broad literature on incubator humidity, the logical next step in gathering what is known and not known about humidification was to conduct a systematic review. This chapter presents a systematic review of RCTs that explores the effect of the level of incubator humidity (higher versus lower) on preterm infant survival and morbidity. The aim of the review was to gather existing evidence and create a critical review of incubator humidity that might inform the proposed clinical trial more effectively than individual studies. I will present the chapter in two parts. The first part explains systematic review methodology and its status within neonatology, justifies the choice of methodology and the decision to conduct the review using the methods of the Cochrane Collaboration, presents the protocol of the systematic review (in PDF format) as published in the Cochrane Library (Sinclair & Sinn 2007) and reflects on its development.

The second part of the chapter presents the completed review (also in PDF format), highlights the challenges encountered during the review process and explores the consequences of these challenges and the implications of the review findings for the proposed study. This section includes my reflection on and learning of a process regarded as the gold standard by removing subjectivity and bias, thus improving rigour. The reader will notice that both the protocol and the review, at times, use a different voice when compared with the work of the thesis.
3.2 Systematic Review and Meta-Analysis

Since the empirical literature is growing at an exponential rate and research results accumulate rapidly, it has become increasingly difficult to interpret what it all means for patient care. Systematic reviews have become an essential tool in improving accessibility to research findings and are considered an essential source of evidence to answer a broad range of questions and guide clinical decisions and health care policy (Fox 2011; Lavis 2009). Although there is criticism of systematic review methodology, it remains at the top of the evidence hierarchy that the majority of clinicians use when determining the strength of evidence of effectiveness.

The purpose of this systematic review was to provide an objective overview of all available evidence on incubator humidity. Introduced and promoted within the framework of evidence-based medicine (EBM), the systematic review retrieves and combines the results of relevant high-quality studies addressing a similar research question. As in any research, and as is evident from our present review, the review process involves the formulation of a question, the collection of data from available primary studies and predetermined eligibility criteria that includes a statement of objectives, materials and methods that are explicit, transparent and reproducible (Egger, Davey Smith & Altman 2001; Glasziou et al. 2001; Greenhalgh 2006). Acknowledging that the systematic review is retrospective by nature (with the exception of prospective meta-analysis) and therefore susceptible to several sources of bias, the methods aim to limit systematic error (bias) and reduce the chance of effect (Higgins & Green 2011). Reducing bias can improve the reliability of findings by applying the same level of rigour to the process of review as is used in any well-conducted and clearly reported primary research.

The summary of existing results from a range of research studies has the potential to create new knowledge and understanding on a given topic. For this reason, although there is no gathering of new data, some researchers consider a systematic review to be more than a review but rather a method of conducting research. The literature refers to this as secondary research - an observational study of the evidence that qualifies for publication as original research in a peer-reviewed journal (Meerpohl et al. 2012).
Publication of the formal comparison of the results of individual primary studies enables clinicians to keep up to date with evidence within their specialty, contributes to resolving uncertainty when the original studies reached differing conclusions, and enables clinicians to draw conclusions and make well-informed decisions about patient care (Klassen, Jadad & Moher 1998). The aim is to reduce the delay in the implementation of effective diagnostic and therapeutic interventions or in expediting the withdrawal of therapies causing harm. In addition to documenting summaries of existing evidence, systematic reviews are powerful tools that identify knowledge gaps in the literature and generate new questions to inform future research agendas. In fact, in some instances, granting agencies require systematic reviews to determine whether there is sufficient justification for the proposed research (Graham 2012).

A systematic review of RCTs may, or may not, include one or more meta-analysis, depending on the suitability of available data. Meta-analysis involves statistical techniques to combine and summarise the results of at least two independent studies in a clinically meaningful way, described by Glass (1976, p. 3) as ‘analysis of the analyses’. Pooling similar studies in a meta-analysis is advantageous because it increases the sample size and thus the power of the analyses; this improves the precision of estimates of treatment effect and assesses whether treatment effects are similar in similar situations (Higgins & Green 2011). Meta-analysis provides the opportunity to address questions relating to specific subgroups that researchers are unable to examine in individual studies of smaller sample size (Ohlsson 1994).

The presence of heterogeneity in study results may mean meta-analysis is not possible or appropriate. Heterogeneity is variation between the estimates over and above the natural sampling variation, that is, the extent to which studies vary from one another. Heterogeneity may be statistical (differences in the reported effects), methodological (differences in study design) or clinical (differences between studies in key characteristics of the participants, interventions or outcome measures) (Moore & McQuay 2006). As will become evident in the following section of the chapter, there was significant clinical and methodological heterogeneity in our systematic review,
which prevented the pooling of primary studies in a meta-analysis; we therefore report
the results narratively.

The ability to increase the power of the analysis in a systematic review is of particular
importance within the field of neonatology. Most of the trials of neonatal interventions
are single-centre studies and are too small to detect treatment effects reliably. Although
meta-analyses can increase statistical power and precision in the estimate of effect size,
the outcomes for which data are available limit this. All too often, the design of RCTs
of neonatal interventions aims to demonstrate the effect of a therapy on surrogate
outcomes (such as PDA) rather than later cognitive and motor function. In addition, the
numerous variables at play (gestation, birth weight, intra-uterine growth restriction,
sepsis and associated medical or surgical conditions) result in heterogeneous samples
that present challenges in determining links between interventions and outcomes with
confidence. Even large trials that include hundreds of infants will not have many infants
of any given weight or gestational age at birth to determine the benefits and risks of
treatment (Tarnow-Mordi, Kumar & Kler 2011). Therefore, the generalisability of trial
results within specific neonatal populations is problematic. Systematic review
methodology is one potential solution to this problem and, in recent years, has become
an accepted method to evaluate neonatal interventions and develop policy and CPG
within the specialty.

3.3 Rationale
3.3.1 For using systematic review methodology

Undertaking a systematic review of the literature that evaluates the effect of humidity
on preterm infant health outcomes prior to conducting the proposed clinical trial had
potential value for the work of the thesis for two reasons. The first reason was that it
would identify what evidence existed and the location of the knowledge gaps, and
assess the appropriateness of the research questions. The second reason was that it
would determine the design features required for development of the most appropriate
and rigorous study.
3.3.2 For using the methods of the Cochrane Collaboration

The primary reason for using the methods of the Cochrane Collaboration to conduct the systematic review was that the Cochrane Database of Systematic Reviews is widely regarded as the single best resource of evidence of the effectiveness of clinical care today. Cochrane systematic reviews are of high quality primarily because each review adheres to the rigorous methodology required by the Cochrane Collaboration, which includes publication of a peer-reviewed protocol before the reviewers conduct the systematic review (Higgins & Green 2011). The reviews report on inclusion and exclusion criteria, assess the quality of the included studies and the consistency of results across trials (in both direction and magnitude of effect), minimise bias, have no language restrictions and allow clinicians and consumers to assess how applicable the findings are to a particular patient population and individual (Klassen, Jadad & Moher 1998; Mulrow 1994; Sacks et al. 1987; Thacker 1998). The Cochrane Collaboration has evolved over time and is today an international network of individuals and institutions that produce systematic, periodically updated reviews of RCTs (Higgins & Green 2011). Given its international success and reputation for high-quality perinatal reviews, of which Australia is a major contributor, conducting the review using the methods of the collaboration seemed an obvious choice. The following section presents the published protocol of the review.¹

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Higher versus lower humidity for the prevention of morbidity and mortality in preterm infants in incubators (Protocol)

Sinclair L, Sinn JKH
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BACKGROUND

Since the study of Blackfan and co-workers in 1953 reported improved outcomes for premature infants in warm humidified environments, those caring for sick neonates have considered the use of warm humidified environments to improve thermal stability and outcome (Blackfan 1953). Incubator humidity itself has increased over the past two decades in response to the increasing number of very low birth weight and extremely premature infants within neonatal intensive care units. Humidified incubators have been used to decrease evaporative losses and thermal instability, improve fluid and electrolyte balance and enhance skin integrity in preterm infants (Hamperl 1985; Rutter 1996; Rutter 1999) during the first few days or weeks of life when transepidermal water loss (TEWL) is at its highest level (Agran 1999; Hammerlund 1986; Nenno 2003; Rutter 1999). Although high levels of humidity are often provided routinely in the management of preterm infants, there is no consensus on the optimal level of humidification required or on the effect of exposure to different levels of humidification over time.

One of the complications of extreme prematurity is the immature infant's limited ability to control body temperature and water balance. Excessive evaporative heat and water loss occurs, in part as a consequence of thin, functionally immature skin that offers little barrier to the postnatal environment (Hamperl 1975; Hammerlund 1982; Hamperl 1985; Rutter 1979). Evaporative loss plays a major role in thermoregulation and fluid balance (Hamperl 1979; Mod 2004; Rutter 1979; Rutter 1996; Gaylord 2001) and constitutes a large part of insensible water loss (Hamperl 1982; Hammerlund 1983; Hammerlund 1986). Thermal management is problematic in the most premature infants in the presence of high evaporative losses. Each milliliter of water that evaporates from the skin results in the loss of 560 calories of heat (Rutter 2000). It can prove difficult to keep these infants warm, even with high inscuator temperatures. To achieve homeostasis it is necessary to create a thermal environment in which the infant's body temperature can be maintained within normal range without increasing both oxygen consumption and metabolic rate. A radiant warmer can provide an adequate heat source, but transepidermal water loss is increased (Hamperl 2001). Incubators heated concomitantly with warm air can create such a microenvironment. However, as the air temperature in a closed incubator is increased, skin temperature and permeability as well as surface evaporation are also increased. Thermal stability is achieved, even in the immature infants, when this microenvironment is humidified.

Achievement of satisfactory fluid and electrolyte balance can also prove challenging for clinicians providing care for extremely premature infants. To prevent hypernatremic dehydration, management must include the prevention of high transepidermal losses or compensating for the large volumes of fluid lost by high infusion rates of intravenous fluids. In a previous Cochrane review (Bell 2001), fluid restriction was shown to decrease the incidence of patent ductus arteriosus, necrotizing enterocolitis and death in preterm infants. Reducing TEWL may contribute to these improved outcomes.

Transepidermal water loss is a continuous passive process. Water diffuses through the skin down a gradient from higher water pressure in the tissues to lower water pressure in the surrounding air. As the immature skin offers little resistance to diffusion and is unable to limit body water loss, transepidermal losses are high. Transepidermal losses decrease with both postnatal and gestational age as the skin matures with exposure to air (Agran 1999; Hammerlund 1986; Yehghorov 1998). TEWL itself may be one of the driving forces behind the maturation process. Although there is a great reduction in TEWL by two weeks of age, researchers suggest that the transient canal may not achieve functional and structural integrity in extremely preterm infants until five to seven weeks postnatal age (Agran 1998; Yehghorov 1998; Yehghorov 1998 suggest 30 week's post conceptual age may be an important milestone in skin maturation irrespective of gestational or postnatal age.

Humidity plays an important role in TEWL. Humidity is described as either absolute or relative humidity. Absolute humidity refers to the actual water vapour content of air. Most often, humidity is expressed as relative humidity (RH), which is the ratio of the actual amount of water vapour in the air to the amount it could hold when saturated, expressed as a percentage (%). Relative humidity varies significantly with changes in temperature; it decreases with increasing temperature even when the actual amount of water vapour stays the same. Increasing the ambient temperature within a microenvironment therefore further increases the potential for both TEWL and evaporative heat loss. RH and TEWL are related to each other in an inverse linear fashion; the addition of supplemental humidity reduces TEWL and evaporative heat loss (Hamperl 1979). Water loss occurs when RH reaches 100% but this can be difficult to achieve and maintain in the clinical setting. A relative humidity of 80 to 90% is achievable and can reduce water loss to one third of the water loss compared to preterm infants receiving 50% humidity (Hamperl 1983). Potentially reducing TEWL, with the provision of supplemental humidity could delay the normal epidermal maturation process. Previous experimental studies have demonstrated increased functional maturation of fetal skin in the animal model following exposure to dry environments (Dendo 1998; Hasley 1997). What this may mean in relation to the extremely preterm infant and the optimal levels of humidity upon maturation remains to be determined.

There are concerns regarding the safety of increased humidity for this vulnerable population. An enclosed environment with a high relative humidity may pose an additional risk for neonatal infection. Neonatal infection is a frequent and sometimes serious complication of neonatal intensive care (Stoll 2002). Extremely premature infants are at increased risk of sepsis due to a poorly developed epidermal barrier, an immunosuppressed state, exposure to
Objective

The objective of the review is to determine the effect of the level and duration of incubator humidity used in the first few days or weeks of life on survival and morbidity of preterm infants.

Primary comparison:
(a) Low versus moderate to high level of humidity
(b) Short versus moderate to long duration of humidity

Secondary comparison:
(a) No humidity versus low level of humidity
(b) No humidity versus moderate level of humidity
(c) No humidity versus high level of humidity
(d) Low level of humidity versus moderate level of humidity
(e) Low level of humidity versus high level of humidity
(f) Moderate level of humidity versus high level of humidity
(g) Short duration versus moderate duration of humidity
(h) Short duration versus long duration of humidity
(i) Moderate duration versus long duration of humidity

Level of humidity:
No humidity, low level of humidity < 65%, moderate level of humidity 65% - 79%, high humidity > 80%

Duration of humidity:
Short 0-7 days, moderate 8-21 days, long > 21 days

Subgroup analysis:
(a) For gestational age: 23-26 weeks vs 27-32 weeks vs 33-37 weeks
(b) For birthweight: < 1000 g vs 1000 g vs 2000 g vs > 2000 g

Methods

Criteria for considering studies for this review

Types of studies
Randomised or quasi randomised controlled trials. Cross-over trials will be included for purposes of defining some of the secondary outcome measures.

Types of participants
All preterm infants (< 37 completed weeks of gestation) who are cared for in an incubator

Types of interventions
No humidity versus low, moderate or high level of humidity (low level < 65%, moderate level 65% - 79%, high humidity > 80% approximately)
Low versus moderate to high humidity (> 65%, moderate humidity 65% - 79%, high humidity > 80% approximately)
Short versus moderate to long duration of humidity (short 0 - 7 days, moderate 8 - 21 days, > 21 days)
Studies with or without compensatory adjustment of water intake, or of air temperature, will be eligible

Types of outcome measures
Primary outcome measures:
(a) Incidence of patent ductus arteriosus treated with indomethacin/aspirin therapy or surgery
(b) Chronic lung disease at 28 postnatal days (oxygen dependency or respiratory support) or at 36 weeks post-menstrual age (oxygen dependency or respiratory support)
(c) Mortality: neonatal death and death during initial hospitalisation

Secondary outcome measures:
(a) Fluid and electrolyte balance
(b) Weight loss or gain
(c) Episodes of hypernatremia (serum sodium > 145 mmol/L) - mean level daily in the first 14 days of life
(d) Transcutaneous water loss as measured by an evaporimeter (g/m²/h) - several measurements over 24 hour periods in first 14 days of life
(e) Skin integrity: severity of cutaneous, urinary, blood or cerebral spinal fluid
(f) Incidence of intraventricular haemorrhage - all haemorrhage (graded according to the criteria of Papile 1978) and severe haemorrhage (including grades 3 and 4 haemorrhage)

Higher versus lower humidity for the prevention of mortality and morbidity in preterm infants in incubators (Protocol)

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(h) Growth and neurodevelopmental outcome in childhood - presence of neurodevelopmental sequelae (i.e., any sensory, motor, cognitive, psychologic or behavioral impairment) reported on follow-up any time after the neonatal period

Search methods for identification of studies

See: Neonatal Group search strategy

The standard strategy of the Cochrane Neonatal Review Group will be used. Electronic searches of the following databases will be conducted:

- The Oxford Database of Perinatal Trials, The Cochrane Central Register of Controlled Trials (most recent issue of The Cochrane Library).
- Data base of Abstracts of Reviews of Effects (DARE 1994 to date).
- MEDLINE (1966 to date).
- Old MEDLINE (pre 1966).
- EMBASE (1974 to date).
- CINAHL (1982 to date).

Previous reviews including cross references, abstracts, conference and symposia proceedings. There will be no constraints based on language or publication status when searching for trials.

Search strategies will be developed using the following keywords/index terms "Infant, prematures", "Prematurity", "Humidity/ humidification", "Body temperature/thermoregulation/heat loss/ hypothermia", "Water loss/transdermal water loss/TWEL/skin integrity", "Infections/humidifiers"

Data collection and analysis

The standard review methods of the Cochrane Neonatal Review Group as documented in the Cochrane Library will be used. Abstracts from the initial search will be read by the primary review author to identify studies that meet the inclusion criteria. Appropriate original full articles will be retrieved and reviewed to determine eligibility. Cited references from retrieved articles will also be searched for additional studies. A second review author will independently search for all potential citations. All relevant articles will be discussed (included or excluded) in the Cochrane Review.

Included trial data will be processed as described in the Cochrane Collaboration Handbook (Cochrane 2006) version 4.2.6.

Data collection & analysis

The systematic review will follow the method described in the Cochrane Collaboration Handbook. Reports under consideration will be evaluated for methodology, quality and appropriateness for inclusion independently by two review authors. Methodological quality assessment will be performed with consideration of four major sources of potential bias and methods of avoidance as follows:

1. Selection bias - blinding of randomisation
2. Performance bias - blinding of intervention
3. Attrition bias - completeness of follow-up

All relevant publications will be reviewed independently by the two review authors. Independently they will extract the outcome data from each report to be included in the meta-analysis. The methodological quality of each trial will be assessed by the two reviewers and comparisons made. Primary investigators will be contacted where appropriate if additional information is required. Discussion will be used to reach consensus between review authors and resolve differing opinions. If necessary, participation of a third person will be sought.

Methods used to synthesize the data:

The data will be collected and analysed with the standard methods of Cochrane Neonatal Review Group. Statistical analysis will be performed using Review Manager software (RevMan 4.2.9) using a fixed effects model. Effects will be expressed as relative risk (RR), risk difference (RD) for categorical data and weighted mean difference (WMD) for continuous data. 95% confidence intervals will be reported. Heterogeneity of the included trials will be tested using an I-squared statistic. To determine whether there is any difference between study results due to plausible effect modifiers, subgroup analysis will be performed (as defined in the Objectives section under pre-specified sub-group analysis), given sufficient numbers for analysis. The analysis will explore the effects of varying levels and duration of humidity in relation to birthweight, gestational age and postnatal age. If heterogeneity exists the source of the variability will be explored. Sensitivity analyses may be performed to evaluate the effect of trial quality. If heterogeneity can be explained by subgroup analysis, the results will be presented in this way. If heterogeneity cannot be explained, individual trial results will be reported.

Acknowledgements

Professor Jackie Crisp, David Cau, Professor of Child & Adolescent Nursing, Faculty of Nursing, Midwifery & Health, UTS Sydney Children’s Hospital, Randwick, Campus Science, University of New South Wales, Australia

Higher versus lower humidity for the prevention of morbidity and mortality in preterm infants in incubators (Protocol)
Additional references

Agera 1998

Agera 2006

Bell 2001

Blackfan 1933

Cochrane 2006

Denda 1998

Flenady 2003

Gaydos 2001

Hammarsd 1979

Hammarsd 1982

Hammarsd 1983

Hammarsd 1986

Hanley 1997

Harpin 1985

Hartnell 2000

Horn 1994

Lyman 2002

Modi 2004

Nonnen 2000

Papile 1978

Rutter 1979

Rutter 1988

Rutter 1996
Bunter 1999

Bunter 2000


Tollien 2001

Yogeshwar 1998

*Indicates the major publication for the study

**WHAT'S NEW**

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**HISTORY**


**DECLARATIONS OF INTEREST**

The authors of this review have no conflict of interest to declare
3.4 The Protocol

3.4.1 Collaboration

The Cochrane Collaboration encourages an interdisciplinary and collaborative approach to research and during the process of review. Accordingly, the first step in the review process was to find a co-reviewer. John Sinn, one of my field supervisors and co-author of several neonatal Cochrane reviews, was an obvious choice. We discussed the proposed review with the chair of the Australasian Cochrane Neonatal Group, who suggested that no-one locally had expertise on this topic and that we should work directly with the Cochrane Neonatal Review Group (CNRG) in the United States.

Before undertaking a systematic review, the Cochrane Collaboration requires the development and publication of a peer-reviewed research protocol that aims to minimise bias (Higgins & Green 2006). The Cochrane Handbook for Systematic Reviews of Intervention 4.2.6 (Higgins & Green 2006), the Quality of Reporting of Meta-Analyses, known as the QUOROM statement (Moher et al. 1999) (later updated to the C checklist) and discussion with the CNRG informed the development of the protocol.

3.4.2 Refining the research question

Careful articulation of the question was the second step in the process because it provides the scope of the review by defining the type of patients, intervention, comparator and outcomes evaluated in the review (Melnyk & Fineout-Overholt 2005; Schardt et al. 2007). The literature refers to this question structure by the acronym PICO (Richardson et al. 2005). Discussion with the CNRG led to the decision that the research question should be sufficiently broad to allow for variations across neonatal populations and to include as many trials of incubator humidity use as possible. Therefore, expansion of the question to include all preterm infants, not solely the subgroup of extremely preterm infants that were the focus of this work, seemed appropriate. Using the PICO and advice from the CNRG, we worked to develop the research question. The CNRG suggested the title ‘Higher versus lower humidity for the prevention of morbidity and mortality in preterm infants in incubators’, which we registered with the Cochrane Collaboration. This clear and focused question enabled the development of eligibility criteria for the review. The Cochrane handbook (Higgins &
Green 2006), the incubator humidity literature, suggestions from the CNRG and my participation in Cochrane Collaboration protocol development workshops informed the development of the protocol, which was published in the Cochrane Library (Sinclair & Sinn 2007).

This first part of the chapter has discussed the use of systematic reviews and meta-analyses in neonatology, justified the choice of methodology, explained the decision to conduct the review using the methods of the Cochrane Collaboration and described the process of protocol development. The second part of the chapter now presents the completed review, reflects on the challenges encountered during the review process and explores both the consequences of these challenges and the implications of the review findings for the proposed clinical trial.
HIGHER VERSUS LOWER HUMIDITY FOR THE PREVENTION OF MORBIDITY AND MORTALITY IN PRETERM INFANTS IN INCUBATORS: A COCHRANE SYSTEMATIC REVIEW

ABSTRACT

Background
Incubator humidity is provided routinely in the management of preterm infants. There is no consensus on the optimal level of humidification required or on the effect of exposure to different levels of humidification over time.

Objectives
To determine the effect of the level and duration of incubator humidity on survival and morbidity in preterm infants in the first few days or weeks of life.

Search methods
The standard search strategy of the Cochrane Neonatal Review Group was used.

Selection criteria
Randomised or quasi-randomised controlled trials enrolling preterm infants to varying levels or durations of incubator humidity.

Data collection and analysis
Independent assessment of the methodological quality of trials and data extraction was conducted by both review authors. Synthesis of data using the standard methods of the Cochrane Collaboration and its Neonatal Review Group.

Results
Four studies enrolling 742 infants were included (Agren, Sjors & Sedin 2006; Sapiegiene et al. 2004; Silverman, Agate & Fertig 1963; Silverman & Blanc 1957). One study compared low level versus moderate level humidity (Agren, Sjors & Sedin 2006) and found a statistically significant increase in transepidermal water loss on days 14 (WMD 9.00 g/m²h, 95% CI 5.08, 12.92) and 28 (WMD 9.00 g/m²h, 95% CI 7.68, 10.32) in low level compared to high level humidity. Three studies compared low level versus high level humidity (Sapiegiene et al. 2004; Silverman, Agate & Fertig 1963; Silverman & Blanc 1957). There was no combining of studies in a meta-analysis due to significant clinical and methodological heterogeneity. Silverman (1957) found a statistically significant reduction in mortality at five days of life (typical RR 0.66, 95% CI 0.46, 0.94) in the high level humidity group. There was no difference in mortality (typical RR 1.22, 95% CI 0.68, 2.17), incidence of intraventricular haemorrhage (typical RR 0.72, 95% CI 0.47, 1.10) or sepsis (typical RR 0.84, 95% CI 0.36,
1.97) at 28 days. Silverman (1963) found no significant difference in mortality at five days (typical RR 1.06, 95% CI 0.81, 1.40) and no difference in mortality (typical RR 0.66, 95% CI 0.26, 1.64), intraventricular haemorrhage (typical RR 1.02, 95% CI 0.70, 1.49) or sepsis (typical RR 0.80, 95% CI 0.39, 1.66) at 28 days. Sapiegiene (2004) reported no significant difference in incidence of patent ductus arteriosus (typical RR 1.57, 95% CI 0.81, 3.06), sepsis (typical RR 1.50, 95% CI 0.83, 2.71) or fluid requirements (WMD 0.60 ml/kg/day, 95% CI -13.9, 14.39) in the first week of life. One study No studies reported on varying durations of humidification. No studies reported outcomes beyond 28 days of life.

**Authors' conclusions**

There is insufficient evidence from clinical trials to guide practice in regarding the optimal levels and duration of incubator humidity for preterm infants. One early study found that high level humidity reduced mortality when compared to low level humidity. However, all infants in the study were hypothermic by today's standards during the study period. Such findings were not repeated in a second study conducted by the same research team when the infants' body temperature was raised, although this second trial did finish early due to local treatment changes. The impact of the humidity on mortality in infants is therefore uncertain. At this time, there is no evidence from randomised controlled trials that humidification reduces fluid requirements, weight loss or incidence of patent ductus arteriosus or increases the risk of intraventricular haemorrhage, sepsis or adverse neurodevelopmental outcomes.

**Plain language summary**

Following preterm birth, heat and fluid are lost through thin and fragile skin. This leads to an inability to maintain body temperature and the regulation of body fluids and salts. Researchers have found that humidifying the environment of preterm babies after birth may be beneficial in reducing this water and heat loss. As a result, incubator humidity use within neonatal intensive care units has increased. A review of the medical literature identified four clinical trials that compared varying levels of humidification involving 742 infants. No trials compared varying durations of humidity use. This review found insufficient evidence to determine optimal levels and duration of humidification or the benefits and risks of use for preterm infants. No trials looked at the effect of humidity on long-term outcomes. Two of the studies were conducted many years ago and findings may not be relevant to today's preterm population. The authors recommend that further trials be performed to answer these important questions. Trials must be large enough to determine the effects of humidity on death or disability.
BACKGROUND

DESCRIPTION OF THE CONDITION

One of the complications of extreme prematurity is the immature infant's limited ability to control body temperature and water balance. Excessive evaporative heat and water loss occurs, in part, as a consequence of thin functionally immature skin that offers little barrier to the postnatal environment (Hammarlund & Sedin 1979a, 1982; Hammarlund, Sedin & Stromberg 1982; Harpin & Rutter 1983; Rutter & Hull 1979). Evaporative loss plays a major role in thermoregulation and fluid balance (Gaylord et al. 2001; Hammarlund & Sedin 1979a; Modi 2004; Rutter & Hull 1979) and constitutes a large part of insensible water loss (Hammarlund & Sedin 1979b; Hammarlund, Sedin & Stromberg 1983; Hammarlund, Stromberg & Sedin 1986; Hartnell, Betremieux & Modi 2000). Thermal management is problematic in the most preterm infants in the presence of high evaporative losses. Each milliliter of water that evaporates from the skin results in the loss of 560 calories of heat (Rutter 2000). It can prove difficult to keep these infants warm even with high incubator temperatures. To achieve homeostasis it is necessary to create a thermoneutral environment in which the infant's body temperature can be maintained within normal range without increasing both oxygen consumption and metabolic rate. A radiant warmer can provide an adequate heat source, but TEWL is increased (Flenady & Woodgate 2009). Incubators heated convectively with warm air can create such a microenvironment. However, as the air temperature in a closed incubator is increased, skin temperature and permeability as well as surface evaporation are also increased. This makes achieving and maintaining thermal stability challenging.

To prevent hypernatraemic dehydration, management must include either reducing TEWL to minimise evaporative losses or compensating for the large volumes of fluid lost by high infusion rates of intravenous fluids. In a recently updated Cochrane review, fluid restriction was shown to decrease the incidence of patent ductus arteriosus, necrotising enterocolitis and death in preterm infants (Bell & Acarregui 2008).

Transdermal water loss is a continuous passive process. Water diffuses through the skin down a gradient from a higher water pressure in the tissues to a lower water pressure in the surrounding air. As the immature skin offers little resistance to diffusion and is unable to limit body water loss, transdermal losses are high. Transdermal losses decrease with both postnatal and gestational age as the skin matures with exposure to air (Agren, Sjors & Sedin 1998; Hammarlund, Stromberg & Sedin 1988; Kalia et al. 1998). TEWL itself may be one of
the driving forces behind the maturation process. Although there is a great reduction in TEWL by two weeks of age, researchers suggest that the stratum corneum may not achieve functional and structural integrity in extremely preterm infants until five to seven weeks postnatal age (Agren, Sjors & Sedin 1998; Kalia et al. 1998). Kalia (1998) suggest 30 weeks' post menstrual age may be an important milestone in skin maturation irrespective of gestational or postnatal age.

DESCRIPTION OF THE INTERVENTION
Humidity plays an important role in TEWL. Humidity is described as either absolute or relative humidity. Absolute humidity refers to the actual water vapour content of air. Most often, humidity is expressed as relative humidity (RH), which is the ratio of the actual amount of water vapour in the air to the amount it could hold when saturated, expressed as a percentage (%). Relative humidity varies significantly with changes in temperature; it decreases with increasing temperature even when the actual amount of water vapour stays the same. Increasing the ambient temperature within a microenvironment therefore further increases the potential for both TEWL and evaporative heat loss. RH and TEWL are related to each other in an inverse linear fashion; the addition of supplemental humidity reduces TEWL and evaporative heat loss (Hammarlund & Sedin 1979b). Water loss ceases when RH reaches 100% but this can be difficult to achieve and maintain in the clinical setting. A relative humidity of 80 to 90% however is achievable and can reduce water loss to one tenth of the water loss compared to preterm infants receiving 50% humidity (Hammarlund, Sedin & Stromberg 1983).

HOW THE INTERVENTION MIGHT WORK
Based on physiological and observational studies, humidified incubators have been used to decrease evaporative losses and thermal instability, improve fluid and electrolyte balance and enhance skin integrity in preterm infants (Gaylord et al. 2001; Harpin & Rutter 1985; Rutter 1996) during the first few days or weeks of life when transepidermal water loss (TEWL) is at its highest level (Agren, Sjors & Sedin 1998; Hammarlund, Stromberg & Sedin 1986; Kalia et al. 1998; Nonato et al. 2000; Rutter & Hull 1979; Telliez et al. 2001).

WHY IT IS IMPORTANT TO DO THIS REVIEW
Since Blackfan and Yagiou (1933) reported improved outcomes for preterm infants in warm humidified environments, those caring for sick neonates have considered the use of warm humidified environments to improve thermal stability and clinical outcome (Blackfan & Yagiou 1933). The use of incubator humidity has increased over the past two decades in
response to the increasing number of very low birth weight and extremely preterm infants within neonatal intensive care units. Although high levels of humidity are often provided routinely in the management of preterm infants, there is no consensus on the optimal level and duration of humidification required or evidence of its effect on neonatal health outcomes.

Potentially, reducing TEWL with the provision of supplemental humidity could delay the normal epidermal maturation process. Previous experimental studies have demonstrated increased functional maturation of fetal skin in the animal model following exposure to a dry environment (Denda et al. 1996; Hanley et al. 1997). What this may mean in relation to the extremely preterm infant and the optimal level or duration of humidification has not been determined.

There are concerns regarding the safety of increased humidity for this vulnerable population. An enclosed environment with a high relative humidity may pose an additional risk for nosocomial infection. Nosocomial infection is a frequent and sometimes serious complication of neonatal intensive care (Kaufman & Fairchild 2004; Stoll et al. 2002; Stoll et al. 2004). Extremely preterm infants are at increased risk of sepsis due to a poorly developed epidermal barrier, an immunosuppressed state, exposure to invasive procedures required for both investigative and therapeutic purposes and a prolonged hospital stay. The design of humidifying systems within modern incubators attempts to reduce sepsis risk. Sterile humidity administered in a gaseous vapour state leaves no airborne water droplets and cannot carry bacteria or other foreign bodies (Lynam & Biagotti 2002). However, the potential for the introduction of external organisms from the hands of caregivers into this warm and moist environment is present. The possible link between humidification and the risk for nosocomial infection in today's incubators remains untested.

**OBJECTIVE**

The objective was to systematically review the evidence to determine the effect of higher versus lower incubator humidity used in the management of preterm infants in the first few days or weeks of life on survival and morbidity.

**METHODS**

The systematic review followed the methods described in the Cochrane Collaboration Handbook (Higgins & Green 2006). The following section presents the methods used to conduct the review.
CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

The eligibility criteria for the review form the basis of the search strategy. The criteria for considering studies for this review relate to the types of studies, participants, interventions and outcome measures.

Types of studies
Two types of studies were eligible for inclusion: randomised controlled trials (where the researchers described the allocation of level of humidification as randomised) and quasi-randomised design studies (if they met the inclusion criteria). Inclusion criteria linked to the research question informed a checklist used to decide which studies were included or excluded.

Types of participants
Included studies were those comprised of preterm infants less than 37 completed weeks of gestation cared for in a humidified incubator.

Types of interventions
Included studies used varying levels and duration of incubator humidification in the management of preterm infants. Discussion with the Cochrane Neonatal Review Group (CNRG) informed these pre-determined criteria for level and duration of humidity. The definitions of levels and duration were:

- No humidity vs. low, moderate or high level humidity (low level < 65%, moderate level 65% to 79%, and high level ≥ 80%).
- Low vs. moderate to high level humidity (low level < 65%, moderate level 65% to 79%, and high level ≥ 80%).
- Short vs. moderate to long duration of humidity (short 0 to 7 days, moderate 8 to 21 days, long > 21 days).

Studies with or without compensatory adjustment of water intake, or of air temperature, will be eligible.

Types of outcome measures
A literature review informed the outcome measures below. Discussion with the CNRG and review of outcome measures following data extraction confirmed significance of outcomes chosen.
Primary outcomes eligible for inclusion include:

a) Incidence of patent ductus arteriosus treated with indomethacin/ibuprofen therapy or surgery
b) Chronic lung disease at 28 postnatal days (oxygen dependency or respiratory support) or at 36 weeks post-menstrual age (oxygen dependency or respiratory support)
c) Mortality: neonatal death and death during initial hospitalisation

Secondary outcomes eligible for inclusion include:

a) Fluid and electrolyte balance
b) Weight loss or gain
c) Episodes of hypernatraemia (serum sodium greater than 145 mmol/L) - mean level daily in the first 14 days of life
d) Transepidermal water loss (TEWL) as measured by an evaporimeter (g/m²h) - several measurements over time
e) Skin integrity as measured daily by a reliable and valid skin assessment scale for preterm infants
f) Incidence of culture positive blood, urine or cerebral spinal fluid
g) Incidence of intraventricular haemorrhage (IVH) haemorrhage will be graded according to the criteria of Papile (severe grades, 3 and 4) (Papile et al. 1978)
h) Growth and neurodevelopmental outcome in childhood - presence of neurodevelopmental sequelae (that is, any sensory, motor, cognitive, psychologic or behavioural impairment) reported on follow-up at any time after the neonatal period

SEARCH METHODS FOR IDENTIFICATION OF STUDIES
Other resources searched included abstracts, and conference and symposia proceedings. Hand searching of key journals aimed to identify potential trials for inclusion. The search also included manual checks of cited references from retrieved papers and the grey literature. There were no restrictions based on country of origin, when the study was undertaken, or publication status. In addition, the primary author contacted two major incubator manufacturers but neither source identified further studies for inclusion.

**APPRAISAL AND SELECTION OF STUDIES**

Two reviewers independently reviewed the titles and abstracts of citations generated by the search to assess their eligibility for further review based on the selection criteria and chose articles for possible inclusion. Both reviewers also independently rated the eligibility of the original full text papers based on the same evaluation strategy using the pre-established criteria and met to compare and discuss results. Discussion and reference to original texts resolved uncertainty related to the inclusion of a study. There was no difference of opinion about the eligibility of studies without requirement of third party consultation. Development of a data extraction tool enabled the collection of relevant data from the identified studies. The reviewers adapted the data extraction template of Juni and colleagues (Juni, Altman & Egger 2001) to achieve this. The tool evaluated the strength of each study’s design, methods, and analysis. Documentation included rationale for excluding studies.

**DATA EXTRACTION AND QUALITY ASSESSMENT**

Both reviewers independently extracted data using the data extraction tool developed for this purpose to ensure accuracy and consistency and avoid transcription errors. Data extracted from each study included: study population; study environment, study methods; interventions; outcome measures; sample size; reported outcomes; adequacy of follow-up; conclusions and limitations of the study. Both reviewers independently assessed the methodological quality of included studies with consideration of four major sources of potential bias and methods of avoidance that included blinding of randomisation (selection bias), blinding of intervention (performance bias), completeness of follow-up (attrition bias), and blinding of outcome assessment (detection bias). The authors independently undertook this assessment and assigned a rating of either Yes (Adequate), Cannot Tell (Unclear), or No (Inadequate) for each according to the methods of the Cochrane Collaboration (Higgins & Green 2006). Each reviewer independently extracted data. The reviewers met to compare findings, differences were resolved through discussion.
METHODS USED TO SYNTHESISE THE DATA

The data was collected and analysed with the standard methods of the Cochrane Neonatal Review Group. Statistical analysis was performed using Review Manager software (RevMan 4.2.9). Effects are expressed as relative risk (RR) and weighted mean difference (WMD). All results reported include 95% confidence intervals. Assessment of sources of potential heterogeneity as defined by Higgins (2008) revealed significant heterogeneity between included studies. In each comparison in this review significant clinical and methodological heterogeneity existed, it was therefore inappropriate to combine study results in a meta-analysis. In addition, publication bias was not assessed as there were fewer than ten included studies. The review reports on each included study individually providing a narrative review rather than statistical analysis.

RESULTS

The following section presents the results of the systematic review. The section includes the results of the search, the number of retrieved studies, the characteristics of included and excluded studies, the quality assessment processes utilised, descriptions of the interventions and outcome measures and the implications for clinical practice and future research.

DESCRIPTION OF STUDIES

Excluded studies

Ten studies were identified as possibly eligible for inclusion in this review. Six studies that compared types of interventions eligible for the review did not meet the inclusion criteria. A tabular summary of the following excluded studies is presented in Appendix? Two cross over studies were excluded as the outcome measures reported (body temperature, apnoea, sleep, respiratory and heart rate) were not part of the outcomes for this review (Belgaumkar & Scott 1975; Telliez et al. 2001). Silverman et al (1958) randomised infants to different ambient temperatures not different humidity levels and the study was excluded. Chao et al (1988) randomised incubators (not infants) to either provide humidity or no humidity irrespective of infant group. The study was excluded as humidity was provided for term infants and those with major congenital anomalies, infants less than 31 weeks gestation at birth were excluded. Miller et al (1961) compared the effects of high versus low level humidity on body temperature and oxygen consumption. The study was excluded as the outcomes measures were not part of the outcomes of this review. In addition, the researchers did not mention method of randomisation. One study, that was published in
German and required translation into English, was excluded as it was a non-randomised physiological study measuring skin and rectal temperatures at both high and low humidity levels (Hanssler & Breukmann 1993).

Translation
Translation was required for one study (Hanssler 1993). A neonatal registrar from Germany employed in the NICU at the time of this review examined the study using the inclusion criteria. The study was excluded from the review for reasons previously discussed. Full professional translation as recommended by Sandford (1996) was therefore not required.

Included studies
Four studies met the criteria for inclusion (Agren 2006, Sapiegiene 2004, Silverman 1957, Silverman 1963). Details of these studies are discussed below.

One study compared low level of humidity versus moderate level of humidity:

**Agren (2006)**
Infants: The gestational age of the participating infants in this study ranged from 23 to 27 weeks gestation.
Intervention: The study compared the effect of low versus moderate level of humidity on postnatal skin maturation in the first 28 days of life. Infants were randomised within 24 hours of birth and all infants received high level of humidity (85%) for the first week of life. On day 7 of life, infants were randomised to one of two study groups (50% or 75% humidity) and maintained in the assigned humidified environment until 28 days of age.
Outcomes: The study reported TEWL and weight change in the first 28 days of life, total daily fluid requirements and serum sodium levels in the first 14 days and incidence of PDA.

Three studies compared low versus high level of humidity:

**Silverman (1957)**
Infants: All preterm infants were participants in this study.
Intervention: This study compared the effects of low (30 to 60%) versus high level humidity (60 to 90%) when incubators are maintained at the same ambient temperature (28.9°C, range 28.3 to 29.4°C). Infants were randomised to low or high humidity from admission for a period of 5 days. The study had six trial arms that included antibiotics:

30 to 60% humidity + penicillin vs 30 to 60% + oxytetracycline vs
80 to 90% humidity + penicillin vs 80 to 90% + oxytetracycline
Then 30 to 60% humidity + oxytetracycline vs 80 to 90% + oxytetracycline

Outcomes: The study reported mortality and incidence of IVH and sepsis during the trial period (less than 5 days) and at 28 days. Diagnosis of both IVH and sepsis was made at post-mortem.

Silverman (1963)

Infants: Participating infants in this study weighed less than 1500g at birth.

Intervention: This study compared the effects of low (30 to 60%) versus high level humidity (80 to 90%) when infants were maintained at the same body temperature (36.1°C ± 0.1°C).
Infants less than 48 hours of age were randomised to low or high humidity from admission for a period of 5 days. Matched pairs design was used and included antibiotics and gammaglobulin (with aim of increasing immunity):

- 30 to 60% humidity + gammaglobulin vs 30 to 60% no gammaglobulin
- 30 to 60% humidity + gammaglobulin + prophylactic antibiotics vs 30 to 60% + gammaglobulin + antibiotics only on clinical indication
- 30 to 60% humidity no gammaglobulin + prophylactic antibiotics vs 30 to 60% no gammaglobulin + antibiotics only on clinical indication
- 80 to 90% humidity + gammaglobulin vs 80 to 90% humidity no gammaglobulin
- 80 to 90% humidity + gammaglobulin + prophylactic antibiotics vs 80 to 90% humidity + gammaglobulin + antibiotics only on clinical indication
- 80 to 90% humidity no gammaglobulin + prophylactic antibiotics vs 80 to 90% humidity no gammaglobulin + antibiotics only on clinical indication

Outcomes: The study reported mortality and incidence of IVH and sepsis during the trial period (less than 5 days) and at 28 days. Diagnosis of IVH and sepsis was made at post-mortem. The study was ceased early due to changes in local practices that could influence the results.

Sapienge (2004)

Infants: Participating infants in this study weighed less than 1000g at birth.

Intervention: This study compared the effects of low level (50 to 55%) versus high level of humidity (80 to 85%) in the first 7 days of life. Infants were randomised at birth to low or high level humidity for a period of 7 days.

Outcomes: Outcome measures for this study included total daily fluid requirements, incidence of PDA and sepsis in the first 7 days of life and incidence of chronic lung disease.
RISK OF BIAS IN INCLUDED STUDIES

Randomisation

_Agren 2006_
Quasi-randomised study. Assignment to an intervention group was by date of birth.

_Sapiegiene 2004_
The researchers did not specify the method of randomisation.

_Silverman 1957_
Quasi-randomised study. Assignment to an intervention group was based on a table of random permutations.

_Silverman 1963_
Quasi-randomised study with matched pair design. Assignment of matched pairs to an intervention group was based on a table of random permutations.

Allocation concealment
The method of allocation concealment was not specified in one study (Sapiegiene et al. 2004). Two studies used sealed envelopes (Silverman, Agate & Fertig 1963; Silverman & Blanc 1957). There was no allocation concealment in one study (Agren, Sjors & Sedin 2006).

Blinding of treatment
All four included studies were unblinded (Agren, Sjors & Sedin 2006; Sapiegiene et al. 2004; Silverman, Agate & Fertig 1963; Silverman & Blanc 1957). It is not possible to blind clinicians to the level of humidity provided.

Blinding of measurement
Blinding of measurement and outcome assessors was not possible in two studies ((Agren, Sjors & Sedin 2006; Sapiegiene et al. 2004) as outcomes were short-term and apparent to all. Blinding of outcome measures was not made explicit in two studies (Silverman, Agate & Fertig 1963; Silverman & Blanc 1957). No study reported long term outcomes.

Adequacy of follow-up
Follow up was considered adequate if < 20%.
Agren 2006:
Twenty-seven infants were enrolled in this study. Five infants were excluded due to chromosomal abnormality (n=1), transfer to other hospitals (n=2) and death (n=2). 18.5% loss to follow-up.

Sapiegiene 2004:
Thirty-nine infants were enrolled in this study. Five infants were excluded secondary to skin infections and congenital heart disease (n=3) and death (n=2). 12.6% loss to follow-up.

Silverman 1957:
This study enrolled three hundred and twenty five infants (193 infants in the first trial period and 132 infants in the second trial period). One defection of unknown reason (n=1). Less than 1% loss to follow up.

Silverman 1963:
This study enrolled four hundred and three infants. Forty-one infants were excluded as they were unmatched (n=9) or mismatched (n=32). 10% loss to follow up.

Adequacy of methodology
There was inadequate randomisation and/or allocation concealment in all four studies (Agren 2006, Sapiegiene 2004, Silverman 1957, Silverman 1963).

EFFECTS OF INTERVENTIONS
Results from a total of 742 infants were available from the four eligible studies with the majority of infants (n =686) enrolled in the two early studies (Silverman, Agate & Fortig 1963; Silverman & Blanc 1957).

NO HUMIDITY VS LOW LEVEL OF HUMIDITY
No studies were eligible that compared these interventions

NO HUMIDITY VS MODERATE LEVEL OF HUMIDITY
No studies were eligible that compared these interventions

NO HUMIDITY VS HIGH LEVEL OF HUMIDITY
No studies were eligible that compared these interventions
NO HUMIDITY VS LOW TO MODERATE TO HIGH LEVEL OF HUMIDITY

No studies were eligible that compared these interventions.

LOW LEVEL VS MODERATE LEVEL OF HUMIDITY (COMPARISON 01)

One study (Agren 2006) compared the effects of low level versus moderate level humidity on postnatal skin maturation in the first 28 days of life.

Transcutaneous water loss

Agren (2006) reported a statistically significant increase in TEWL on day 14 (WMD 9.00 g/m²h, 95% CI 5.08, 12.92) (Outcome 01.01) and day 28 of life (WMD 9.00 g/m²h, 95% CI 7.68, 10.32) (Outcome 01.02) in the infants in the low level humidity group compared to the infants in the moderate level humidity group.

LOW LEVEL VS. HIGH LEVEL OF HUMIDITY (COMPARISON 02)

Three studies (Sapiegiene et al. 2004; Silverman, Agate & Fertig 1963; Silverman & Blanc 1957) compared the effects of low level versus high level of humidity on short term outcomes. Two studies (Silverman, Agate & Fertig 1963; Silverman & Blanc 1957) compared the effects of low level versus high level humidity on mortality, incidence of IVH and sepsis on days five and 20 of life. One study (Sapiegiene et al. 2004) compared the effects of low level versus high level humidity on incidence of PDA, sepsis and fluid requirements in the first seven days of life.

Mortality

Silverman (1957) reported a significant decrease in mortality within the first 5 days of life in the infants receiving high level humidity (typical RR 0.66, 95% CI 0.46, 0.94) (Outcome 02.01) but no significant difference in mortality by day 28 (typical RR 1.22, 95% CI 0.68, 2.17) (Outcome 02.02). Silverman (1963) reported no significant decrease in mortality within the first 5 days of life (typical RR 1.06, 95% CI 0.81, 1.40) (Outcome 02.03) or by day 28 in the infants receiving high level versus low level humidity (typical RR 0.66, 95% CI 0.26, 1.64) (Outcome 02.04).

Neonatal morbidity

Intraventricular haemorrhage

Silverman (1957) reported no significant difference in incidence of IVH (typical RR 0.72, 95% CI 0.47, 1.13) (Outcome 02.05). Silverman (1963) reported no significant difference in incidence of IVH (typical RR 1.02, 95% CI 0.70, 1.49) (Outcome 02.06)
**Sepsis**

Sapiegiene (2004) reported no significant difference in incidence of sepsis (typical RR 1.5, 95% CI 0.83, 2.71) (Outcome 02.07). Silverman (1957) reported no significant difference in incidence of sepsis (typical RR 0.84, 95% CI 0.36, 1.97) (Outcome 02.08). Silverman (1963) found no significant difference in the incidence of sepsis (RR 0.80, 95% CI 0.39, 1.66) (Outcome 02.09).

**Patent ductus arteriosus**

One study (Sapiegiene et al. 2004) found no significant difference in the incidence of clinically significant FDA in the first 7 days of life (typical RR 1.57, 95% CI 0.81, 3.06) (Outcome 02.10).

**Fluids and electrolytes**

Two studies (Agren, Sjors & Sedin 2006; Sapiegiene et al. 2004) included fluids and electrolytes as outcome measures. Agren (2006) reported no statistical significance in fluid requirements between the two study groups but this was depicted in figure format only with no mathematical calculation provided. Similarly, differences in daily serum sodium levels were not statistically significant. Sapiegiene (2004) also reported no significant difference in fluid requirements (WMD 0.60 ml/kg/day, 95% CI -13.9, 14.39) between the two groups (Outcome 02.11).

**Weight loss**

Two studies (Sapiegiene et al. 2004; Silverman & Blanc 1957) reported no significant difference in weight loss (described in papers only, no data). There was a reported trend towards increased weight loss in infants who received low level humidity (37 ± 27 g/day) compared to those who received high level humidity (33 ± 25g/day) in another study (Silverman & Blanc 1957) but this was not statistically significant.

**Mild to moderate level of humidity vs high level of humidity**

No studies were eligible that compared these interventions

**Low level of humidity vs moderate to high level of humidity**

No studies were eligible that compared these interventions

**No studies reported on varying durations of humidity**
DISCUSSION

This review examines evidence from randomised controlled trials to determine the optimal level and duration of incubator humidity in the management of preterm infants and the effects of use on clinically important outcomes. Four studies or abstracts were eligible for inclusion in the review (Agren, Sjors & Sedin 2006; Sapiegiene et al. 2004; Silverman, Agate & Fertig 1963; Silverman & Blanc 1957). All included studies reported humidity use in the management of preterm infants. Three studies were published; one of those did not complete recruitment due to clinician attrition. The fourth study was incomplete and published in abstract form only. The majority of studies were of poor methodological quality and significant clinical and methodological heterogeneity meant that no results were pooled in a meta-analysis.

One study in this review (Agren, Sjors & Sedin 2006) compared the effects of moderate level versus low level humidity on skin maturation. The evidence from this study suggests that TFWL was higher on day 14 and more pronounced by day 28 of life in infants in the moderate level humidity group compared to those in the low level humidity group. This finding may be contrary to popular belief. Physiological studies using serial measurements of TEWL over time have revealed that TEWL is highest during the first few days after birth, decreases with increasing postnatal age and is reduced in a humidified environment even in the most preterm infants (Agren, Sjors & Sedin 1998; Hammarlund & Sedin 1979a; Harpin & Rutter 1983; Wilson & Maibach 1980; Wu & Hodgman 1974). For this reason, humidity use is increasing in the management of preterm infants.

In explanation of the study findings, Agren (2006) postulated that moderate levels of humidity over time might delay epidermal barrier maturation resulting in the persistent high levels of TEWL observed. This suggestion appears to support previous experimental studies that described increased functional maturation of fetal skin in the animal model following exposure to a dry environment (Denda et al. 1986; Hanley et al. 1997). What delaying the epidermal barrier maturation process means for this population of infants is unknown. This work suggests that not only level but also duration of humidity may be important. No studies assessed the effects of varying durations of humidity on outcomes.
The earliest study (Silverman & Blanc 1957) reported a statistically significant decrease in mortality within the first five days of life in the infants in the high humidity group when compared to infants in the low humidity group. The researchers explained this increase in survival as the result of the increase in body temperature observed in the infants in the high humidity group. All infants in this study were however hypothermic by today’s standards. In a subsequent studies reported by the same research team (Silverman, Agate & Fertig 1963; Silverman, Fertig & Berger 1958) when there was no significant difference in mortality between the two groups in the first five days of life when body temperatures were maintained at 36°C. The inference here is that the increase in body temperature rather than the level of humidity per se positively influenced outcomes in the first study (Silverman & Blanc 1957). Of note, is that there was no difference in mortality at 28 days in this first study.

Mortality rates were high at the time of both Silverman studies included in the review and outcomes measured were reported at post-mortem. Not all infants who died had a post-mortem. Post-mortem was undertaken in 75% of deaths in the low level humidity group and in 86% in the high level humidity group in the early study (Silverman & Blanc 1957) and in 93% of deaths in the low humidity level group and 89% in the high level humidity group in the later study (Silverman, Agate & Fertig 1963). Reported rates of IVH and sepsis may therefore be inaccurate. Further, it is unclear how differences in antibiotic and immunoglobulin use affected health outcomes.

One study (Silverman, Agate & Fertig 1963) terminated early due to the introduction of new therapies that made it difficult to ensure the matching of pairs of infants; this increases the risk of asserting significance or non-significance erroneously. Both Silverman studies were conducted in a pre-surfactant and antenatal steroid era when neonatal mortality was higher and extremely preterm infants rarely survived. Results are therefore not generalisable to today’s preterm infant population.

Sapijgene (2004) also found no significant difference in incidence of sepsis in infants who received high level humidity compared to the low level humidity group in the first week of life. However, this study was not completed and not adequately powered to detect differences in outcomes. No study compared incidence of sepsis in a humidified environment versus a non-humidified environment. While observational studies have previously reported increased nosocomial infection and colonisation of pathogens (Chao, Hsieh & Hwang 1989; Sever 1959; Verissimo et al. 1990) in infants within humidified microenvironments, there is no robust evidence of increased sepsis risk within today’s modern incubators as no randomised controlled trials have been conducted.
Perhaps somewhat surprisingly, two studies (Agren, Sjors & Sedin 2006; Sapiegiene et al. 2004) found no difference in fluid requirements and weight loss between the study groups. Observational studies have described a reduction in fluid requirements because of reduced transpidermal water losses in highly humidified environments (Gaylord et al. 2001; Locke et al. 2000). Small sample sizes in both studies may explain these findings. Similarly, both studies (Agren, Sjors & Sedin 2006; Sapiegiene et al. 2004) reported no difference in incidence of PDA. The incidence of chronic lung disease, although to be evaluated in one study (Sapiegiene et al. 2004), was not reported.

The review found some evidence of an increase in TEWL over time in moderate levels of humidity when compared to low levels of humidity (Agren, Sjors & Sedin 2006). It has found no evidence of a decrease in weight loss or fluid requirements or an increase in incidence of PDA, sepsis, IVH or mortality in moderate or high level incubator humidity when compared to low level incubator humidity. The review has highlighted a clear lack of robust research into the benefits and risks of humidification.

**Limitations of the Review**

Major limitations of the review include the limited number of studies and the small number of infants enrolled in trials incorporated in the review resulting in limited power to detect clinically important effects on the specified outcomes. No studies were available to provide data on any long-term outcomes. No randomised studies directly compared varying durations of humidity. No studies compared humidity versus no humidity.

**Limitations of the Studies**

There was inadequate randomisation and/or allocation concealment in all studies (Agren 2006, Sapiegiene 2004, Silverman 1957, Silverman 1963). Two of the included studies were performed in the 1950s and 1960s (Silverman, Agate & Fertig 1963; Silverman & Blanc 1957). There have been many changes in clinical care and in the characteristics of the preterm infant population since these studies were undertaken. Many of these changes may render the results redundant and difficult to generalize to today’s population of preterm infants. One study reported an interim analysis in abstract form only (Sapiegiene et al. 2004). Only 39 infants from a calculated sample size of 60 were enrolled. Outcomes for all studies were short-term (up to 28 days of life); no long-term data were available. Agren et al (2006) reported a statistically significant increase in TEWL on days 14 and 26 in moderate
versus low level humidity. The sample size of this study was small which may have influenced outcome measures.

AUTHORS’ CONCLUSIONS

IMPLICATIONS FOR PRACTICE

Although there has been increasing use of incubator humidity in the management of preterm infants, this review highlights a lack of evidence from randomised controlled trials to guide clinical practice in relation to optimal levels and duration of incubator humidity for preterm infants. One early (1957) study found that high level humidity reduced mortality when compared to low level humidity. However, all infants in the study were hypothermic by today’s standards during the study period. Such findings were not repeated in a second study conducted by the same research team when the infants’ body temperature was raised, although this second trial did finish early due to local treatment changes. The impact of the humidity on mortality in infants is therefore uncertain. At this time, there is no evidence from randomised controlled trials that humidification reduces fluid requirements, weight loss or incidence of patent ductus arteriosus or increases the risk of intracranial haemorrhage, sepsis or adverse neurodevelopmental outcomes. One small study suggests that a moderate level of humidity over time may increase TEWL and delay epidermal barrier maturation. The effect of delayed barrier maturation on preterm infants is unknown.

IMPLICATIONS FOR RESEARCH

Further multisite well-conducted trials with adequate power and randomisation procedures to measure the effect of humidity on both short term and long-term health outcomes are required to make the systematic review more powerful before optimal levels and durations of humidification and potential benefits and risk of use can be determined. In particular, it may be prudent to consider the duration of humidity use and the level of humidity over time in future research.

ACKNOWLEDGEMENTS

Professor Jackie Crisp, David Coe Professor of Child & Adolescent Nursing, Faculty of Nursing, Midwifery & Health, UTS & Sydney Children’s Hospital, Randwick, Conjoint Professor University of New South Wales, Australia
Dr Patrick Flosdorff translated the excluded German study into English
REFERENCES


Rutter, N. & Hull, D. 1979, ‘Water loss from the skin of term and preterm babies’, *Archives of Disease in Childhood*, vol. 54, no. 11, pp. 858-68.


So far, in this second part of the chapter I have presented a systematic review of RCTs. The results of the review support the findings of the broad review of the literature presented in Chapter 2: optimal levels and duration of humidity have not been determined for infants of varying gestational ages and the effect of humidification on clinically important outcomes is not clear. In the following section, I reflect on my experience of the systematic review process and the challenges encountered, and discuss the implications of these challenges and the results of the review for the proposed study.

3.5 Reflections, Learning and Critical Questions

Peer review is a key part of the review process; qualified independent researchers control the reviewers’ methods, results and publication. To receive the assistance and guidance of world-renowned neonatal experts in the CNRG was an exciting prospect for me. In fact, some of the individuals involved were the authors of the first evidence-based neonatal textbook. The authors published the textbook at the time when I commenced my career in neonatal nursing, and this text was my neonatal ‘bible’ for many years. In addition, at that time, I was working with one of my current clinical supervisors of this thesis, who has espoused EBP and the value of large clinical trials since that time. I learnt much and contributed to some international trials in a small way. Exposed to this methodology during my first years as a neonatal nurse, I became very familiar with the RCT, hence, my enthusiasm to conduct an RCT as part of my doctorate. Given this background, my enthusiasm for the opportunity to conduct the systematic review under the guidance of this eminent group of neonatologists was explicable. Of note, a member of this peer review group was also the current editor of the CNRG. However, the reality of collaborating with the CNRG was somewhat different from my perhaps naïve expectations.

Engaging with the Cochrane Collaboration processes proved challenging. As mentioned previously, we published the protocol for the review in 2007 (Sinclair & Sinn 2007). We submitted the first draft of the full systematic review to the CNRG two weeks following publication of the abstract. Distance, busy schedules and time differences delayed responses from the CNRG over time; sometimes there was a 12- to 18-month wait time on feedback. One skill I had to cultivate was patience. Although I
acknowledged that the Cochrane Collaboration was undergoing significant rapid growth and simultaneous restructure (the development of the ‘Archie’ database) during this time, delay in feedback proved challenging. I sent frequent emails to the CNRG and later engaged the Australasian Cochrane Group to aid the process. The last contact I had with the CNRG was through the chair of the Australasian group. Despite the inclusion of all previous comments from the CNRG in the final version that we submitted (as above), there was a lack of consensus on the results of the review by member(s) of the CNRG and a suggestion from the group that we change the research question (the question was actually one that the CNRG had proposed, approved and previously published). However, there was uncertainty over what the new review question should be, and the words ‘prevention of morbidity and mortality’ were deleted from the title of the review. Comparisons suggested included ‘high’ versus ‘low’ humidity, ‘early’ versus ‘late’ humidity, ‘body temperature controlled’ versus ‘not body temperature controlled’ and ‘fluid intake controlled’ versus ‘fluid intake not controlled’. These comparisons were confusing, especially given that we had agreed previously not to include body temperature as an outcome of the review and because researchers rarely include local fluid management strategies when reporting study results. This is currently the situation at the time of writing this chapter - the review remains unpublished.

The systematic review process, which I enjoyed immensely from a learning perspective, was one that later caused much frustration and angst. The following is my reflection on and understanding of events that occurred. Feedback from the CNRG stated that there was demonstrated evidence of the benefits of incubator humidity use in the management of preterm infants. Literature used to support this statement has already been included in this thesis; one study is an RCT that was included in the systematic review (Silverman & Blanc 1957) and the others were small physiological studies. I have already discussed the fact that small physiological studies form the basis of the evidence for humidity use, but physiological studies are not included in a systematic review of RCTs. Further, as previously described, although the study by Silverman and Blanc (1957) demonstrated that high-level humidity reduced mortality in the first five days of life (no difference by day 28), the same research group did not find reduced mortality in two subsequent trials that maintained the infants’ body temperature at 36 °C (Silverman, Agate & Fertig 1963; Silverman, Fertig & Berger 1958). Prior to the conduct of these studies, clinicians
had believed that hypothermia was of benefit to newborn infants. The researchers themselves proposed that their work suggested that it was raising the body temperature (either by providing heat or by adding high-level humidity) that improved preterm infant survival and concluded that humidity may not be necessary.

Given the feedback from the CNRG and my status as a novice reviewer, I questioned my own skills. I sought advice from a librarian in a medical library in a major tertiary hospital. The librarian conducted a database search, but retrieved no new RCTs related to incubator humidity. I again reviewed the literature I had retrieved previously, but this repeat review did not change my findings or conclusions. Completing the review left me with many more questions than it had answered, including questions about the peer review process itself. Given the push for EBP, I felt, at least in this instance, that there is little support for the process.

Editors of academic journals are gatekeepers who influence the publication of research. It appears that there are few insights into the peer review process or the reasoning of reviewers. Why would a research question already agreed and published in a Cochrane protocol need to change? More than one member of the CNRG had published on the topic of thermoregulation in preterm infants. Could it be possible that the current establishment rejected the review findings because of individual beliefs about humidity? The rhetoric on systematic review processes is that reviewers conduct reviews in such an objective and rigorous way that they exclude subjectivity, bias and vested interests. The reality may be something quite different; this work questions the motivation of review groups and suggests that systematic reviews may also be open to bias and individual opinion.

Puzzled, I explored the literature for examples of the experiences of others. Bachand and Sawallis (2003) found that the peer review process was variable across journals and disciplines, and other authors described it as slow, unreliable, inconsistent and potentially biased (De Vries, Marschall & Stein 2009). Following high-profile cases that have raised questions about the effectiveness of peer review in ensuring the quality of published research, McCook (2006), Smith (2006) and Henderson (2010) discussed peer review in medical journals. The authors highlighted flaws and biases within the
process and made recommendations for improvement. It would appear that there is less rigour applied to the peer review process than is expected of reviewers’ reports. What then does this mean for EBP? This subject requires further investigation.

Overall, working in collaboration with the individuals involved was much more complex than I had anticipated. Feedback from the CNRG was puzzling, and attempts to discuss my concerns and gain clarity on the group’s expectations were futile. It is my intention to pursue this review with the CNRG beyond the work of the thesis. On reflection, collaborating with a local and already established group of Cochrane reviewers would have been more beneficial to me as a novice reviewer and might have brought about a very different outcome. On a positive note, I thoroughly enjoyed the actual process of review and the learning throughout. Publication of the protocol has also been a useful networking exercise and has revealed many clinicians both nationally and internationally who are interested in improving humidification practices and in future collaboration.

The work outlined and the lessons learned in this present chapter led to a major rethink of my initial intention to pursue an RCT. The systematic review confirmed the lack of evidence on the use of humidity identified in Chapter 2. The questions posed at the end of Chapter 2 remained unanswered however; the appropriate ‘next step’ was less than obvious. What specific research questions should I ask? Which outcome variables should I include? Which of the potential outcome variables should be primary and which should be secondary outcome variables? How do I determine this? Discussion within the supervisory group then centred on study design and outcome measures. After much debate, we decided that, because most single-centre studies are too small to detect treatment effects reliably and the most important outcomes of neonatal care are cognitive and motor function, the study needed to be powered sufficiently to detect these longer term health outcomes. The decision to use death or survival with major disability at two years corrected for gestation as the primary outcome measure would require a large sample size and therefore necessitate the design of a multicentre clinical trial. I was unsure at this time what such a decision meant for my doctoral work. Perhaps I should expect to limit my goals and focus on undertaking a pilot study to test the feasibility and gain greater insight into what a multicentre study would involve.
3.6 Chapter Summary

This chapter has presented the protocol and the actual systematic review titled ‘Higher versus lower humidity for the prevention of morbidity and mortality in preterm infants in incubators: a Cochrane systematic review’. Further, the chapter provided my rationale for using systematic review methodology, summarised the process of systematic review, presented the findings and implications for clinical practice and made recommendations to guide future research. The results of the systematic review suggested that we need further research to reduce the level of uncertainty currently present about humidification practices. Little research assesses the benefits or risks associated with incubator humidity use in the management of extremely preterm infants. Methodologically sound, adequately powered clinical trials with meaningful outcomes are required to raise the power of systematic reviews and guide clinicians in the management of infants in humidified incubators. Subsequent discussions about the work concluded that we ought to design and conduct a large multicentre trial to meet these requirements. I will discuss the implications of this decision later in the thesis.

The chapter also presented reflections on my experiences of the systematic review process. I learnt much about the systematic review but questioned whether the process, which proved to be much more complex than I had anticipated, is as robust as portrayed; individuals may influence the outcomes of review and subsequent publications. This could have implications for EBP and patient care.

The systematic review presented in this chapter provided little robust evidence to inform humidification practices. Given this finding, the one question that arose consistently during supervisory group discussions was related to current practices surrounding humidification use across Australia and New Zealand given the void of clear evidence to support the ‘best’ approach. We hypothesised there would be wide variation in humidification practices across NICUs given the lack of clear evidence to inform practice. There is anecdotal evidence of widespread use of incubator humidity, but it is unclear what factors influence decisions determining humidity use in clinical practice. Therefore, the next logical step in this work was to access neonatal clinicians, gain an understanding of how they use humidity and determine what drives its use.
From this premise, the following chapter of the thesis reports the results of a telephone survey that explored current practice and clinicians’ views on humidity use in NICUs across Australia and New Zealand.
Chapter 4: C’ing the Prejudice in Practice:  
Characters in Context  

* A Survey of Humidification Practices in Australia and New Zealand  

4.1 Chapter Overview  

Given the inconsistencies in practice, the variable use of CPGs and the controversies surrounding the use of incubator humidity in my workplace, as well as the lack of good quality evidence to direct practice, I was motivated to discover how clinicians used humidification in other NICUs. This chapter presents the results from a survey of incubator humidity practices in NICUs across Australia and New Zealand. The survey sought to reveal not only how neonatal nurses use humidity in the absence of clear evidence but also to explore their views and experiences of humidification and the use of CPGs. The chapter is presented in two parts. The first part presents a paper on the survey results that we published in the *Journal of Paediatrics and Child Health* (Sinclair, Crisp & Sinn 2009). The reader will notice that the paper, presented as published, does on occasion use a different voice when compared with the work of thesis. The second part of the chapter explains the methods used, expands on the findings of the survey beyond that of the published paper and presents analysis of qualitative data that provides a more detailed description of the nurses’ views and experiences of using humidity in everyday practice. Finally, I discuss the implications of the survey findings for the proposed clinical trial.
VARIABILITY IN INCUBATOR HUMIDITY PRACTICES IN THE MANAGEMENT OF PRETERM INFANTS

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ABSTRACT

Aim: To determine current practice and opinion in relation to incubator humidity use in the management of preterm infants in neonatal intensive care units (NICUs) within the Australian and New Zealand Neonatal Network (ANZNN).

Methods: A survey was conducted in 26 NICUs in the ANZNN. A senior clinical nurse in each perinatal centre participated in a telephone survey that focused on local humidification practices and on the clinicians’ views and experiences of humidity use.

Results: All centres routinely used supplemental humidity in the management of preterm infants. The majority of centres (77%) had written protocols to guide practice. Eighty-eight per cent commenced humidity at a high level (relative humidity ≥ 80%). There was wide practice variation in the gestational age parameters determining humidification use (all gestational ages up to 37 weeks), duration of use (3 to 77 days), timing of initiation (admission to 72 hours after birth), and weaning practices. Perceived benefits of humidification included improved thermoregulation, skin integrity, and fluid and electrolyte balance and reduced transpidermal water loss. Perceived risks included sepsis and hyperthermia.

Conclusions: Our study confirmed that incubator humidity is used routinely in the management of preterm infants in the ANZNN. Wide variation in humidification practices across NICUs reflects the paucity of research evidence. Perceived benefits and risks of humidity use were consistent with available literature. To optimise the care environment and provide an evidence base for practice further research is warranted.

Key words: incubator humidity; infant; preterm.

INTRODUCTION

There is anecdotal evidence of widespread use of incubator humidity in the management of preterm infants within NICUs. Despite increasing use and reported short-term benefits of humidification, optimal levels and duration have not been defined and there is virtually no
evidence of the effect of humidity on long-term health outcomes. Given the dearth of rigorous research, it is unclear what factors influence decisions determining humidity use in clinical practice. It is important, therefore, to examine existing humidification practices, explore the perceived benefits and risks of use, and understand the challenges for clinicians posed by the lack of evidence.

Because the early studies of Blackfan and Yaglou (1933) and Silverman and colleagues (Silverman, Agate & Fertig 1963; Silverman & Blanc 1957; Silverman, Fertig & Berger 1956) reported improved outcomes for preterm infants in warm humidified environments, there has been interest in the use of incubator humidity. Based on physiological and observational work, the major argument for using humidity is to improve thermal stability, fluid and electrolyte balance, and skin integrity by reducing evaporative heat and water loss from the skin (Agren, Sjors & Sedin 1998; Gaylord et al. 2001; Hammarlund et al. 1977; Hammarlund et al. 1979; Hammarlund, Sedin & Stromberg 1983; Harpin & Rutter 1985; Takahashi, Hoshi & Nishida 1994). Inability to optimise the care environment to achieve and maintain thermal stability and an adequate fluid balance is associated with significant morbidity, especially in the most preterm infants (Bell & Acarregui 2008; Day et al. 1964; Elliot & Mann 1957; Glass, Silverman & Sinclair 1968; Pomerance & Madore 1974; Silverman, Fertig & Berger 1958; Sinclair 2002).

Transdermal water and heat loss is highest in the most preterm infants immediately after birth and reduces with increasing post-natal and gestational age as the skin matures (Agren, Sjors & Sedin 1998; Hammarlund et al. 1979; Hammarlund & Sedin 1982; Hammarlund, Sedin & Stromberg 1983; Kalia et al. 1998; Nonato et al. 2000; Rutter & Hull 1979; Sedin, Hammarlund & Stromberg 1983; Wilson & Maibach 1980). High incubator temperatures used in an attempt to reduce heat loss not only raise the infant’s body temperature but also decrease humidity within the incubator. Heat, in the presence of low-level humidity, increases skin permeability and surface evaporation, further increasing the potential for transepidermal heat and water loss (TEWL). As the relationship between TEWL and humidity is an inversely linear one, evaporative losses can be reduced with the provision of high-level humidity (relative humidity (RH) > 80%) (Agren, Sjors & Sedin 1998; Hammarlund, Sedin & Stromberg 1982; Wilson & Maibach 1980). However, evidence has yet to emerge in relation to the optimal level of humidity over time. One small study suggests that the provision of moderate levels of humidity (70%) beyond 14 days of age delays epidermal maturation, thus increasing TEWL (Agren, Sjors & Sedin 2006). Similarly, optimal duration of humidification has not been defined, reflecting the uncertainty in the literature as to when
complete maturation of the extremely preterm skin occurs and whether it is necessary to humidify the environment until barrier function is fully developed.

Potential risks of humidification include sepsis (Edmondson et al. 1966; Harpin & Rutter 1985; Hoffman & Finberg 1955; Reinartz et al. 1966; Sever 1959; Verissimo et al. 1990) and hyperthermia (Harpin & Rutter 1985). Both are associated with adverse neonatal outcomes (Gunn & Bennet 2001; Newton & Watkinson 2003; Stoll et al. 2004). While prolonged periods of high humidity may theoretically increase the risk of nosocomial infection, there is little mention of humidity as a causative factor in recent literature. The risks of hyperthermia are less well described than those of hypothermia in the preterm infant population.

A recent Cochrane review identified four clinical trials (Agren, Sjörs & Sedin 2006; Sapiegiene et al. 2004; Silverman, Agate & Fertig 1963; Silverman & Blanc 1957) involving 742 preterm infants that compared the effects of varying levels of humidification on neonatal health outcomes (L Sinclair and J Sinn, unpublished data 2009). There is no evidence that incubator humidity use reduces fluid requirements, weight loss, or incidence of patent ductus arteriosus or increases the risk of intracranial haemorrhage, sepsis, or mortality. No studies have compared varying durations of humidity or reported long-term outcomes in relation to humidity use. It would appear that further research is required to optimise humidification practices and determine the benefits and risks of use.

Against this background, the major aim of our study was to determine current practice and examine existing protocols in relation to humidity use. The study also aimed to explore the views of neonatal nurses on the benefits and risks of humidification, the factors influencing decisions in relation to humidity use, and the challenges posed by the lack of robust research. Given the lack of evidence to guide practice we hypothesised that there would be variation among NICUs across Australia and New Zealand.

MATERIALS AND METHODS

DESIGN
Perinatal centres in Australia and New Zealand that routinely provide care for preterm infants from birth were eligible for study inclusion. A structured telephone interview was conducted with a senior neonatal nurse in each centre.

PARTICIPANTS
Participants were senior members of the neonatal nursing team such as clinical nurse consultant, nurse educator, clinical nurse educator or equivalent senior nurse who had knowledge of current clinical practices.

SURVEY INSTRUMENT
In order to gain maximum participation a survey was developed that could be used in telephone interviews. The survey instrument was a questionnaire designed specifically for this study by the authors. The questionnaire covered the range of issues surrounding local humidification practices such as criteria for use, level and duration of humidity and the perceived benefits and risks.

PROCEDURE
Approvals were obtained from the relevant human research ethics committees. NICUs were identified through the ANZNN. An initial telephone discussion determined a senior nurse with knowledge of local humidification practices within each centre. Once identified, each nominated clinician received a personal email inviting him or her to participate in the survey. The email package included a letter of introduction, a participant information leaflet, a consent form and a copy of the interview questions. Follow-up emails and telephone calls maximised timely responses. The primary author, who is also a clinical nurse consultant within an NICU, conducted telephone interviews between January 2006 and January 2007. Respondents were encouraged to discuss their own experiences of local guidelines and humidification practices within their clinical area following completion of the questionnaire. Duration of interviews varied from 20 to 50 minutes.

ANALYSIS
Simple percentages were used to describe current practice in relation to incubator humidity use. Further qualitative information regarding individual participants’ experiences and opinions of current practice provided additional data. Responses were grouped according to the major themes identified.

RESULTS
Twenty-nine centres within the ANZNN provide intensive care for infants. Twenty-six are perinatal centres that routinely provide care for preterm infants from birth and were eligible for inclusion in the study. Three centres were excluded as they are children’s hospitals and
do not routinely provide care for this infant population. Following consent, all nominated neonatal nurses completed the telephone interview.

Table 1 describes the local humidification practices of the participating NICUs; all 26 centres humidified the microenvironment in the management of preterm infants. Supplemental humidity has been a standard of care for more than 5 years in 17 centres (65%). However, six centres (23%) had no written protocol to guide practice in relation to humidity use. Although incubators manufactured by Dräger were most commonly used (73%), almost half of all centres used models designed and supplied by more than one manufacturer. One unit (4%) did not routinely use incubators but rather provided humidity via a plastic tunnel on an open care system under an overhead radiant warmer.
Table 1. Humidification practices of participating NICU's, N=26

<table>
<thead>
<tr>
<th>Criteria for use based on</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age</td>
<td>20</td>
</tr>
<tr>
<td>Birthweight</td>
<td>6</td>
</tr>
<tr>
<td><strong>n=20</strong></td>
<td></td>
</tr>
<tr>
<td>Criteria for use by gestational age (weeks)</td>
<td></td>
</tr>
<tr>
<td>&lt; 28</td>
<td>9</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>5</td>
</tr>
<tr>
<td>&lt; 32</td>
<td>3</td>
</tr>
<tr>
<td>&lt; 34</td>
<td>2</td>
</tr>
<tr>
<td>&lt;37</td>
<td>1</td>
</tr>
<tr>
<td><strong>n=6</strong></td>
<td></td>
</tr>
<tr>
<td>Criteria for use by birthweight (grams)</td>
<td></td>
</tr>
<tr>
<td>&lt; 1000</td>
<td>4</td>
</tr>
<tr>
<td>&lt; 1500</td>
<td>2</td>
</tr>
<tr>
<td><strong>n=26</strong></td>
<td></td>
</tr>
<tr>
<td>Timing of commencement</td>
<td></td>
</tr>
<tr>
<td>NICU admission</td>
<td>3</td>
</tr>
<tr>
<td>&lt; 6 hours</td>
<td>17</td>
</tr>
<tr>
<td>7-24 hours</td>
<td>5</td>
</tr>
<tr>
<td>24-48 hours</td>
<td>1</td>
</tr>
<tr>
<td>Level of initial humidity (%)</td>
<td></td>
</tr>
<tr>
<td>&gt; 80</td>
<td>23</td>
</tr>
<tr>
<td>70-79</td>
<td>2</td>
</tr>
<tr>
<td>Unmeasured</td>
<td>1</td>
</tr>
<tr>
<td>Duration of humidity (days)</td>
<td></td>
</tr>
<tr>
<td>&lt; 7</td>
<td>4</td>
</tr>
<tr>
<td>7-14</td>
<td>7</td>
</tr>
<tr>
<td>15-28</td>
<td>8</td>
</tr>
<tr>
<td>&gt; 28</td>
<td>7</td>
</tr>
<tr>
<td>Duration of humidity based on</td>
<td></td>
</tr>
<tr>
<td>Postnatal age</td>
<td>23</td>
</tr>
<tr>
<td>Weight gain</td>
<td>3</td>
</tr>
<tr>
<td>Timing of weaning (days)</td>
<td></td>
</tr>
<tr>
<td>No weaning</td>
<td>2</td>
</tr>
<tr>
<td>&lt; 7</td>
<td>15</td>
</tr>
<tr>
<td>7-14</td>
<td>6</td>
</tr>
<tr>
<td>&gt; 14</td>
<td>3</td>
</tr>
<tr>
<td>Typical humidity level days 14-28 of life</td>
<td>n=15</td>
</tr>
<tr>
<td>&lt; 70%</td>
<td>9</td>
</tr>
<tr>
<td>&gt; 70%</td>
<td>6</td>
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</tbody>
</table>
The humidification practices of participating NICUs are summarised in Table 2. Gestational age at birth was the most common criterion for humidity use. The median gestational age at commencement was 28 weeks. Where the criterion for use was birth weight, this was categorised as <1000 g or <1500 g. Seventy-seven per cent of centres commenced humidity within six hours of birth. The majority of centres set humidifiers to provide high-level humidity initially; this ranged from 80 to 100% depending on the type and capability of the incubator used. One unit (4%) did not measure the level of humidity provided.

Duration of humidity use ranged from three to 77 days with a median of 28 days. Duration was depended on attainment of a pre-specified postnatal age (23 centres (88%)) or weight gain (three centres (12%)). Of the 15 centres that provide humidity for more than 14 days, six centres (40%) usually provide humidity levels ≥70% beyond day 14 of life. Weaning from high-level humidity to a lower maintenance level appeared to be common practice, with the majority of centres commencing weaning within 14 days. Weaning practices varied, with three centres (12%) using the weaning protocol of the Dräger Computer Heat Balance Program.

<table>
<thead>
<tr>
<th>Table 2: Characteristics of participants’ NICUs, N=26</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICUs using humidity</td>
</tr>
<tr>
<td>Humidification guideline</td>
</tr>
<tr>
<td>Humidity in use (years)</td>
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<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Incubator type</td>
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<td></td>
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<tr>
<td>Incubator manufacture*</td>
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<td></td>
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</tbody>
</table>

* 46% NICUs use a combination of incubator types

There was consensus among participants on the perceived benefits, risks and complications of humidification as illustrated in Table 3. By far the most common benefits reported were
improved thermal stability and fluid balance, but participants stated that improved skin integrity and reduced TEWL and weight loss were also important. The participants identified sepsis and hyperthermia as potential risks of humidity use. Complications of humidity use most commonly reported included the presence of rainout or condensation in 15 centres (58%) and the non-adherence of monitoring equipment in nine centres (35%). Rainout, prolonged periods of high-level humidity and long duration (any level of humidity) were factors that influenced sepsis concern.

<table>
<thead>
<tr>
<th>Benefits</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermal stability</td>
<td>23</td>
</tr>
<tr>
<td>Improved fluid balance</td>
<td>6</td>
</tr>
<tr>
<td>Reduced TEWL</td>
<td>16</td>
</tr>
<tr>
<td>Improved skin integrity</td>
<td>16</td>
</tr>
<tr>
<td>Reduced weight loss</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risks</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>12</td>
</tr>
<tr>
<td>Hyperthermia</td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Complications</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rainout</td>
<td>15</td>
</tr>
<tr>
<td>Non-adherence of equipment</td>
<td>9</td>
</tr>
<tr>
<td>Loss of skin integrity</td>
<td>8</td>
</tr>
<tr>
<td>Cedema/fluid overload</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reasons for sepsis concern</th>
<th>n=12</th>
</tr>
</thead>
<tbody>
<tr>
<td>High level humidity</td>
<td>8</td>
</tr>
<tr>
<td>Long humidity duration</td>
<td>6</td>
</tr>
<tr>
<td>Rainout</td>
<td>11</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The results of our survey confirmed that incubator humidity use has become an accepted practice in the management of preterm infants within NICUs and, as hypothesised, revealed wide variation in humidification practices. Variations in practice were not surprising given the dearth of literature exploring optimal levels and duration of humidity, potential benefits and risks of use or its effect on long-term health outcomes.
The majority of NICUs have used incubator humidity for more than five years. However, six of the 26 centres had no articulated policy or protocol to guide practice. Participants described the anecdotal nature of existing protocols or guidelines and the variability in the extent to which clinicians (both nursing and medical) adhered to them. A lack of available evidence was reported to contribute to variations in practice. Participants stated that individual clinician preferences, experiences, beliefs, and perceived benefits and risks of use as well as infant needs were observed to be significant contributors to many of the decisions made around humidification use and ultimately therefore to clinical practice.

There was also wide practice variation across NICUs in relation to the criteria used to determine humidity use, the time taken to initiate therapy, the duration of use and weaning practices. By far the most important criterion reported to determine humidity use was gestational age. Although all centres humidified the environment in the management of extremely preterm infants, some provided humidity for infants of varying gestational ages up to 37 weeks gestation. Variation in the timing of initiation of humidification was also evident. While most centres (77%) commenced humidity within six hours of birth (usually following stabilisation and arterial and venous catheterisation), humidity was not commenced in some centres until much later, sometimes commencing up to 72 hours after birth. Evidence suggests that TEWL is highest immediately after birth and that high-level humidity is required as soon as possible after birth to reduce large evaporative losses (Agren, Sjors & Sedin 1998; Hammarlund & Sedin 1979a; Hammarlund, Sedin & Stromberg 1982; Hammarlund, Sedin & Stromberg 1983; Kalia et al. 1998; Nonato et al. 2000; Rutter & Hull 1979; Wilson & Maibach 1980).

Variation in the duration of humidity use ranged from three to 77 days. Duration of use was linked primarily to attainment of various pre-specified postnatal ages, often irrespective of gestational age at birth. Such differences in practice are not surprising given there are no studies that compare varying durations of humidification for infants of differing gestational ages.

Weaning was commenced anywhere between three and 28 days with no consensus among participants on timing or what constituted an optimal low maintenance level of humidity. Three centres (12%) used the Dräger Computer Heat Balance Program. The use of this programme, which calculates the required humidity level and weaning schedule based on gestational age, birthweight, and post-natal age, has previously been described in the literature (Lyon & Oxley 2001). Discussion with participants revealed that the weaning process demanded active management of the environment and close monitoring of body
temperature; simultaneously increasing the incubator temperature as the humidity level is reduced maintains thermal stability and prevents hypothermia.

This study found consensus across NICUs around the use of levels of humidity at the higher end of the range (RH ≥ 80%) and in the perceived benefits and risks of use. Humidity levels ≥ 80% were used in the management of extremely preterm infants in the first days or weeks after birth in the majority of centres. This is consistent with available evidence from physiological studies (Hammalund et al. 1977; Hammalund & Sedin 1979b; Harpin & Rutter 1985; Takahashi, Hoshi & Nishida 1994). Six centres provide humidity levels ≥ 70% beyond 14 days of life. Further research is required to determine whether such levels of humidity over time are associated with an increase in TEWL and a delay in epidermal barrier maturation as reported by Agren and colleagues (Agren, Sjors & Sedin 2006). Serum sodium levels, skin integrity, fluid and electrolyte balance, and thermoregulatory state were reported to determine the level of humidity over time and the duration of humidity use in some centres.

Agreed perceived benefits of humidification included improved thermoregulation, fluid and electrolyte balance, skin integrity, and reduced TEWL and weight loss. Risks of use included the potential for sepsis and hyperthermia. Participants reported that rainout was a frequent complication of high-level humidity. Rainout occurs when the canopy temperature is lower than the incubator air temperature. The resultant moist skin increased concern for infection risk. Other predictors for sepsis concern included the provision of high levels of humidity for prolonged periods and the provision of humidity (any level) for the longest durations. There was however, consensus among participants that the perceived short-term benefits of humidity use outweighed potential risks.

**STUDY LIMITATIONS**

We acknowledge potential limitations of the study. We accept that the overall survey results reflect the experiences and opinions of one senior neonatal nurse in each NICU and we have no way of ascertaining the views of clinicians (both nursing and medical) who were not involved in our survey. We were, however, delighted with the 100% response rate and did achieve representation from nurses with diverse clinical backgrounds from all NICUs in the ANZNN. This leads us to believe that neonatal nurses consider the topic addressed in our survey to be important and relevant to everyday practice.
CONCLUSION

In summary, the results of our survey provide insight into humidification practices within NICUs in Australia and New Zealand. We have established that the provision of humidity is part of routine care in the management of preterm infants in all NICUs. As hypothesised, we identified significant differences in practice both across and within institutions, reflecting the lack of research to guide clinicians. Our findings demonstrate that current practices are for the most part consistent with the available literature and that variations reflect the existing gaps within. Our study illustrates that what is required is to establish new knowledge to guide clinicians and optimise the delivery of humidity in the management of preterm infants. Specifically, optimal levels and duration of humidification need to be defined and future trials need to be powered to detect clinically important differences in long-term neurodevelopmental and behavioural outcomes. The participants in this survey voiced overwhelming support for such a study.

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birth-weight infants with neonatal infection. Journal of American Medical Association,* 
So far, in this chapter, I have presented the findings from the survey of humidification practices in a paper that was published in a peer-reviewed journal. I will now present a more in-depth description of the methods used and describe the participants’ views and experiences of humidification that were not included in the published paper because of the limitations of journal requirements, particularly in relation to work length.

4.2 Materials and Methods

4.2.1 Design

I was interested not only in obtaining facts about incubator humidity use but also in exploring clinicians’ experiences of humidification; therefore, the method chosen to collect data was the telephone interview. Alternative methods considered included online questionnaires and face-to-face interviews. The desire to obtain the stories behind the participants’ experiences that might provide insight into humidity use ruled out the use of an online questionnaire. Although face-to-face interviews may have been preferable to improve the quality of both the interaction and the data obtained (Barriball et al. 1996; Chapple 1999; Opdenakker 2006; Rubin & Rubin 2005; Sweet 2002), time, financial constraints and the vast geographical areas involved prevented feasibility of the face-to-face interview option.

I consulted the literature to determine the appropriateness of the telephone interview for this purpose. Some evidence does support the use of telephone interviews as an effective method of data collection (Carr & Worth 2001; Musselwhite et al. 2007) and has suggested that it is as effective in eliciting sensitive information as face-to-face interviews and computer-assisted self-interviews (Bernhardt et al. 2001; Cachia & Millward 2011; Ellen et al. 2002; Sturges & Hanrahan 2004) while allowing access to participants across large geographical areas (Barriball et al. 1996; Opdenakker 2006). Further, Novick (2008) suggested the telephone interview may have some advantages over the face-to-face method by allowing participants to feel relaxed and able to disclose sensitive information more freely. I felt satisfied that the telephone interview was an appropriate data collection method to meet the study objectives.
The survey utilised a semi-structured interview design - the most widely used interviewing format for qualitative research (DiCicco-Bloom & Crabtree 2006). The interview based on the study’s central focus allowed for the standardisation of some questions to establish facts about incubator humidity use to increase the reliability of data and allow comparison of practices across NICUs. A more flexible and open-ended approach for the remaining survey questions enabled participants to reflect on their feelings and beliefs about incubator humidity in the practice setting.

I chose thematic analysis as the method of analysis. Thematic analysis is a data reduction and analysis strategy by which qualitative data are segmented, categorised, summarised and reconstructed in a way that captures and reports the important concepts or themes within the dataset in relation to the aims of the study (Ayres 2008; Braun & Clarke 2006). I chose to use this method because it can provide rich data (Braun & Clarke 2006; Fereday & Muir-Cochrane 2006) and is independent of any particular epistemology or discipline (Braun & Clarke 2006; Tuckett 2005). The method allowed me to report accurately and comprehensively the experiences and views voiced by the participants in relation to incubator humidity use that I captured during the interview process. The analysis section will now detail how I applied thematic analysis to the survey data.

4.2.2 Context and participants

Purposeful sampling techniques identified both sample size and participant selection. This type of non-probability sampling provided useful data with which to meet the aims of the survey. Maximum variation sampling, a purposive sampling technique that allows researchers to explore the common and unique manifestations of a target phenomenon across a broad range of phenomenally and/or demographically varied cases (Sandelowski 1995) informed my decision to seek a sample size that permitted coverage of all 26 eligible NICUs in Australia and New Zealand. For the purpose of this survey, the required sample consisted of one participant from each of the 26 NICUs within Australia and New Zealand.
I used critical case sampling—another form of purposive sampling—to identify participants most likely to provide meaningful information in answer to the study questions (Hansen 2006). Neonatal nurses’ responsibilities include management of the thermal environment and fluid balance, and therefore, they play a pivotal role in the provision of incubator humidity. Nurses are also in an excellent position to provide information about local care practices and, consequently, were the obvious choice to participate in the survey.

In different states across Australia and in New Zealand, neonatal nurses with similar appointments have very different position descriptions. For example, in NSW, a clinical nurse consultant (CNC) might be the most appropriate person with whom to discuss clinical practice issues, whereas a CNC in Western and South Australia has a managerial role with budget responsibilities and may be less familiar with the use of guidelines and their effect on local practices. Consequently, an initial telephone call determined one senior nurse with knowledge of humidification practices and CPG use within each NICU and deemed most appropriate to participate. On occasion, some nurses approached others to invite them to participate, for example, a colleague with a specific interest in incubator humidity. This initial contact allowed a relationship to be established before the distribution of emails requesting participation in the survey. Table 1 shows the nursing position held by each of the participants.

Table 1: Position Description of Participants (N = 26)

<table>
<thead>
<tr>
<th>Position</th>
<th>No.</th>
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<tbody>
<tr>
<td>Clinical nurse consultant</td>
<td>9</td>
</tr>
<tr>
<td>Nurse educator</td>
<td>3</td>
</tr>
<tr>
<td>Clinical nurse educator</td>
<td>7</td>
</tr>
<tr>
<td>Nurse unit manager</td>
<td>3</td>
</tr>
<tr>
<td>Clinical nurse specialist</td>
<td>4</td>
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</table>

Once identified, I sent the 26 nominated nurses a personal email inviting them to participate in the study. The email package included a letter of introduction that explained the purpose of the interview, a participant information leaflet, a consent form and a copy of the interview questions. I sent the interview questions in advance for two reasons. First, in a meta-analysis of studies that used mail and face-to-face surveys as research methods, De Leeuw and colleagues (2007) found advance letters to be
effective in raising participant response rates. Second, with the intention of enriching responses, I hoped an advance copy of the interview questions might enable time for participants to reflect on local practices and personal experiences of incubator humidity use before the interview. However, there is no empirical basis to support the assumption that doing so will provide richer data. Follow-up emails and telephone calls maximised timely responses.

4.2.3 Survey instrument

The questionnaire design met the needs of the study and enabled both the gathering of information about incubator humidity use within NICUs and participants’ views of and experiences of its use (see Appendix 1). The literature review and systematic review presented in Chapters 2 and 3 in combination with multidisciplinary group discussion informed the content of the questionnaire. Questions used in the survey sought to elicit information about humidification practices such as criteria for use, level and duration of humidity, perceived benefits and risks, and specific local and demographic data. Additional questions provided participants with the opportunity to describe experiences, thoughts and feelings about humidification in their own words. Given that there was no previous validation, the questionnaire required testing.

4.2.4 Pilot testing

Using similar subjects, the same setting and the same techniques of data collection and analyses as the proposed study, I recruited four senior neonatal nurses to participate in pilot interviews. The pilot test had two aims. The first aim was to determine if there were flaws, limitations or other weaknesses within the survey design and allow any revisions prior to the implementation of the study (Kvale 2007). The second aim was refinement of my interview technique. To determine content validity, a debriefing session with colleagues following the piloting process confirmed that the questions elicited information that was congruent with the survey objectives. Analysis of the results enabled the rewording of two questions to avoid repetition and ambiguity. The opportunity to rehearse enabled me to gain confidence in my technique, and interviews became easier over time as I became familiar with the sequence of questioning and the
use of questions that would prompt, probe and encourage responses when applicable. This process of testing and review undoubtedly improved the quality of the interviews.

4.3 Procedure

4.3.1 Ethical considerations

Ethical considerations relevant to this survey related to issues of consent, privacy and confidentiality, risks to participants and data storage. The relevant university (2005-172R) and health service (2005/9/6.3 (2202)) scientific and human research ethics committees (HRECs) provided approval for the survey. All nurses approached consented to participate in the survey and were advised that they could withdraw their consent at any time during the survey without any effect on relationships or the NICU involved. Although risk is present in all research, the risks to participants in this survey were minimal.

The data were stored securely to ensure maximum privacy for participants. A locked filing cabinet stored all the participants’ data. A separate filing cabinet maintained the security of any documents or data that named or identified individual nurses or NICUs to protect confidentiality. I stored the data in a secure filing cabinet and on password-protected computer files in my office; only I had access to the data files. After seven years, all survey data will be destroyed in accordance with the National Health and Medical Research Council’s (NHMRC) National Statement on Ethical Conduct in Research Involving Humans of the (NHMRC 2007).

4.3.2 Interviews and data collection

I conducted the telephone interviews between January 2006 and January 2007. It was important to be flexible and conduct the interviews at a time most convenient to the participants (Smith 2005), and on occasion, at their own request, interviews occurred when the participants were at home to remove the distraction of unpredictable workloads or potential interruptions in the NICU. Understanding the importance of developing a positive relationship with the participants to allow a richness of data to be uncovered (McConnell-Henry et al. 2009–10), I built a rapport with each participant.
before the interview to set them at ease and encourage open discussion; this introduction included a review of the aims of the survey. I hoped that developing a good rapport might increase the level of support for both the proposed study and its outcomes by engaging clinicians—albeit in a small way—from the beginning.

Asking the same questions of all participants guided discussion and provided broad structure to allow for comparison of humidification practices across the sample. Additional questions that emerged from the dialogue between the participants and me provided scope to explore topics identified by the participants. I took detailed notes throughout the interviews after preparing the participants for pauses that might occur during the conversation to facilitate this. Additional notes served as a reminder of the need to return to a question or topic that might provide more rich data, especially when the conversation had changed, rather than interrupt the flow of the conversation. Participants reflected on their own practice and that of others, provided insight into local clinical settings and included any additional information they considered relevant to the objectives of the survey or wished to share. They were very keen to discuss issues about humidity use they had encountered and provided information freely. Lively and animated discussion ensued as the participants described their experiences, the challenges faced and anecdotes about humidity use. It became clear early in the discussions that incubator humidity was an emotive subject and one that initiated much debate among clinicians within NICUs.

I gave the participants feedback following the interview (McConnell-Henry et al. 2009–10) and disengaged gently to avoid causing the participants to feel exploited or that their disclosure might in some way affect them in the future (Borbasi et al. 2002; Kavanaugh & Ayres 1998). I thanked the participants, assured them that their contribution was invaluable to the work and provided them with the opportunity to have any questions they might have answered. Discussion included the intention to present the survey findings to the participants and the Perinatal Society of Australia and New Zealand (PSANZ) Annual Scientific Congress, and to submit a manuscript for publication. I also gave assurance of confidentiality in any presentation of the data.
I hurriedly wrote additional reflective notes following each interview to improve accuracy of recall (Smith 2005) while adding my own thoughts of the proceedings. Each page of written records contained a participant identifier to ensure accuracy. I did not record the interviews because it was not the intention to conduct in-depth analysis. Although this might imply that some information was missing in the final interpretation and presentation of the findings, I believe that extensive note taking and the use of clarifying questions in the case of ambiguity did capture most of the information relevant to the aims of the study.

4.4 Analysis

Thematic analysis is a process for encoding qualitative information (Boyatzis 1998). I used inductive thematic analysis, in which themes are derived from the participants’ discussions, to interpret individual participants’ experiences and opinions of humidity (Boyatzis 1998; Miles & Huberman 1994). Braun and Clarke’s (2006) six phase process guided much of the analysis (see Table 2), and Saldana’s coding manual informed the coding of data (Saldana 2009). I analysed the data using a semantic approach, that is, I identified themes from the ‘explicit or surface meanings of the data’ (Braun & Clarke 2006, p. 84) rather than at a latent level that aims to identify underlying ideologies or ideas that govern what participants say.
Table 2: Thematic Analysis of Survey of Humidification Practices

<table>
<thead>
<tr>
<th>Phase One: Becoming familiar with the data</th>
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<tr>
<td>The aim of this first phase was to provide a view of neonatal nurses’ reality within the NICU in relation to incubator humidity use and to gain familiarity with the data. My systematic reading and re-reading of the text identified comments and topics of interest. I took field notes throughout.</td>
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<th>Phase Two: Generating initial codes</th>
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<td>Phase two involved the grouping of responses that shared the same characteristics and the devising and assigning of coding categories to these groups. This involved me really thinking about the data, creating connections and giving brief verbal descriptions (words and phrases) to semantic features of data that appeared interesting or addressed the same topics or themes that were meaningful to the survey questions. The preliminary codes based on one interview enabled the development or modification of codes following analysis of the data from subsequent interviews. Saldana’s (2009) coding manual aided clarity on code development. I coded and identified the themes and then discussed the analysis with my supervisor. This process allowed for consistency in the method but did not permit alternative perspectives from a variety of people with differing expertise, which is an obvious limitation.</td>
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<th>Phase Three: Searching for themes</th>
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<tr>
<td>A theme refers to a cluster of linked categories that convey similar meanings and relate to the aims of the survey. In this phase, I read the data and initial coding categories again, identified areas of similarity or patterns within those categories and contemplated how different codes might combine to form a theme (Braun &amp; Clarke 2006). This process involved writing coded categories on Post-it notes and repositioning them around a board until relationships or significance were identified and, later, the development of a thematic map. In this phase, I placed quotations and concepts that fitted together into broader themes. This phase identified potential survey themes and subthemes.</td>
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<th>Phase Four: Reviewing themes</th>
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<tr>
<td>Phase four involved placing all the themes and subthemes together and confirming that the proposed themes had adequately captured the coded data. Themes either related to the survey questions or appeared frequently and were therefore considered important. The themes became categories for interpretative analysis.</td>
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<th>Phase Five: Defining and naming themes</th>
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<tr>
<td>The aim of phase five was to define and confirm the name of each theme and check the accompanying narratives from the dataset for accuracy and relevance. Since this was a simple analysis, no further refining of the themes was required. Analysis identified four major themes.</td>
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<th>Phase Six: Producing the report</th>
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<tr>
<td>This phase included reporting and discussing the results (see following section below).</td>
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4.5 Results

As mentioned previously, all 26 senior neonatal nurses (100%) participated in the survey. Interview duration varied from 20 to 50 minutes (median 37.5 min). Several participants stated they had consulted with colleagues prior to the interview, and their responses included the views of others; this finding supports my decision to present the survey questions to the participants in advance of the interview. Synthesis of the participants’ responses to questions about humidification practices identified one overarching theme: uncertainty in the practice environment. Other major themes identified were working with humidity in practice, working with evidence and guidelines and context of practice. Figure 1 depicts the thematic map created from the
results. I will now present the results under these identified themes; my use of descriptive elements and participant quotes provide definition and add clarity.

4.5.1 Uncertainty in the practice environment

Analysis revealed an overarching and multidimensional theme—uncertainty in the practice environment, which is evident in the following sections. The lack of rigorous evidence to support clinical decisions, inconsistencies in practice, challenging professional relationships and characteristics of the workplace collectively contributed to this uncertainty and revealed further the challenges for clinicians working in the environment.

4.5.2 Working with humidity in practice

Since the published paper presented the findings of this theme in part one of the chapter, to avoid repetition, I will not include it again here.
4.5.3 Working with evidence and guidelines

The results of this survey established variability in how clinicians work with evidence and the extent to which they use CPGs to inform practice. Although some participants reported ‘no problems’ with the interpretation of evidence and the development and use of guidelines within their clinical environment, the majority recounted many examples of the uncertainty and conflict that failure to standardise practice can cause. The majority of participants said that a humidification guideline did exist; however, for some, its development had proved to be problematic because of the lack of clear evidence and failure to achieve local consensus to inform its content. The following quotation reflects the challenges imposed by the lack of research to inform practice: ‘We developed a guideline…but little evidence…still don’t know what level [of humidity] is best or when to stop…not ideal…difficult when teaching others when no evidence’ (C2). Participants from the six NICUs that had no articulated guideline for humidity use described the consequences of this: ‘We have no guideline so whether it [humidity] starts or stops varies from day to day’ (J1). ‘We have no policy for weaning it’s just stopped and the baby gets cold…freezing sometimes’ (B3).

Opinion was split over the extent to which clinicians accepted and utilised existing incubator humidity guidelines. A number of participants stated that nurses liked to use the guideline and generally viewed it positively. In contrast, other participants described a very different experience of CPG use: ‘There is a guideline but most don’t use it, they don’t use most of the guidelines…practice here depends on the consultant on service’ (N5). ‘We have a guideline…some follow it’ (G3). Concerns about sepsis risk appeared to cause the greatest variability in guideline use: ‘Some of us are worried about infection’ (J1). ‘I don’t agree with the current protocol…we humidify for weeks…what about infection we know it’s bad for preterm brains…our infection rates are the worst in the state I think’ (M3). ‘We had two 24 weekers with candida from the humidity we stopped using it [humidity] for a while after that’ (F4). Another criticism of guideline use was the inability to individualise care according to patient need. The following quotation reflects a typical response: ‘care is not individualised, they [preterm infants] all receive the same level of humidity for the same length of time irrespective of gestation or weight’ (N6).
4.5.4 Context of practice

The results of the survey revealed elements of the context in which the practice of incubator humidity occurs. The context of the practice environment was a key theme identified as affecting the use of humidity and patient care. Three subthemes identified within the context of practice were *inconsistencies in humidification practices*, *individuals and their relationships*, and *staffing and skill mix*.

4.5.4.1 Inconsistencies in practice

The survey results demonstrated inconsistencies in humidification practices, both across and within NICUs, as a common theme. Participants reported that individual clinician preferences, experiences, beliefs and perceived benefits and risks (mostly concern about sepsis risk) were significant contributors to many of the decisions made about humidification use. The following comments captured this sentiment and revealed that differences in decision making created confusion, anxiety and unpredictability: ‘*There’s no consensus everybody does something different*’ (D3). ‘*One neonatologist here believes humidity should never be higher than 40% at any time...what are we supposed to do?’* (T3). ‘*It is unacceptable to have to change care plans and charts every time a different consultant is on call, usually they haven’t even looked at the baby*’ (N4). Similarly, humidification practices sometimes varied depending not only on medical management but also on the manager or senior nurse on duty: ‘*Staff have to check who is on before making the decision to start [humidity] or not...on one shift it’s the right thing to do on the next it’s not...it can be stressful, how must this affect the bubs [babies] long term?’* (H4). This apprehension about the effect of inconsistency on health outcomes reflected the concerns of other participants. The following comment highlights the potential for the disruption of nurse-family relationships: ‘*I know they [nurses] find it all very frustrating and it’s embarrassing when talking to parents...what must they think when we change practice with every consultant shift change...what is this doing to patients...nurses feel awful...suggests poor care...and is very stressful, emotionally draining*’ (S5). Although the focus of this survey was the use of humidity,
participants alluded to the fact that inconsistencies in other care practices existed: ‘It’s not just humidity, they [consultants] don’t agree on lots of practices’ (C2).

4.5.4.2 Individuals and their relationships

The survey results revealed that in the majority of NICUs, individuals—not CPGs— influenced the use of incubator humidity. Individual beliefs and characteristics and ‘who was working’ on any given shift (nursing or medical) influenced the quality of the interactions, decision making and, ultimately, patient care. Participants described strained workplace relationships and stated how difficult it was, especially for more junior nurses, to deal with and work with the challenges of inconsistency and uncertainty. When the approach taken was hierarchical and offered little opportunity for team discussion, nurses chose the path of least resistance: compliance—providing care as ordered, to avoid conflict. One participant highlighted this point: ‘Just do what they [consultants] say...avoid the grief...it’s not worth it...[nurses] need to stay safe’ (T2).

4.5.4.3 Staffing and skill mix

Unpredictable workloads, poor nurse staffing levels and insufficient numbers of experienced staff contributed to uncertainty in the practice environment. The participants described nurse staffing levels and skill mix within the NICU as variable and often unsatisfactory. The following responses highlight concerns raised by a number of participants about the effect of low nurse staffing levels, poor skill mix and the resultant lack of supervision and appropriate education for junior nurses on patient care: ‘Staffing is critical at times [low numbers and poor skill mix] and the young ones [junior nurses] are left to look after very preterm babies...they don’t know how to look after them or how to use humidity...body temps [temperatures] are sometimes all over the place’ (L3). ‘They [junior nurses] forget to turn the temp [incubator temperature] up...there is just not enough supervision... sometimes not enough senior staff per shift. Some of us have complained nobody listens’ (S1).
4.6 Discussion

This survey reported how clinicians use incubator humidity in NICUs across Australia and New Zealand and has provided insight into decision making, the context of the practice environment and neonatal nurses’ views and experiences of humidity use. For consistency, I will discuss the results using the key themes identified above.

4.6.1 Uncertainty in the practice environment

Uncertainty was inherent in everyday practice. The survey found numerous factors that contributed to this uncertainty: a lack of robust evidence to inform humidification practices, inconsistencies in care practices, autocratic decision making and difficult relationships, a complex and stressful environment, the unpredictability of the daily workload, the inability to predict treatment effects and longer term health outcomes, poor staffing and skill mix, and poor leadership. An increasing amount of published work describes uncertainty, especially within intensive care environments for nurses, doctors and families (Allred et al. 1994; Gerrity et al. 1995; Greco & Roger 2003; Healy & McKay 2000; Kipnis 2007; Penrod 2001; Scott et al. 2008; Turner, Tomlinson & Harbaugh 1990).

The findings from this survey reflect those described by Scott et al. (2008). Scott and colleagues explored the organisational context of a single paediatric intensive care unit to understand the process by which context influenced nurses’ research utilisation behaviours. The authors identified three factors that created uncertainty in this practice environment: inconsistency in management, the unpredictability of nurses’ work and the complexity of working with other disciplines. The researchers stated that no previous work had reported inconsistency in management and the complexity of working with other disciplines as sources of uncertainty. This present survey concurs with the findings of Scott et al.

Perhaps it is time to acknowledge and address uncertainty in the workplace. Evidence suggests uncertainty has consequences for clinicians, which manifest as emotional responses such as stress (Gray-Toft & Anderson 1981; Greco & Roger 2003; Healy &
McKay 2000), high blood pressure (Greco & Roger 2003), mood disorders (Healy & McKay 2000), poor performance (Salyer 1995) and burnout (Garrett & McDaniel 2001). In the current climate of nursing shortages, it is important to recognise and work constructively with factors that affect nurses and have the potential to affect retention. The literature has previously identified uncertainty as one of the factors that contribute to parent stress in the NICU (Callery 2002; Obeidat, Bond & Callister 2009; Shin & White-Traut 2007).

This work suggests that uncertainty is intrinsic within the NICU environment. Since it is unlikely that uncertainty within the NICU can be reduced, we need to consider ways to deal with uncertainty to lessen its effect on both clinicians and families.

4.6.2 Working with humidity in practice

As previously mentioned, the published paper discussed the findings of this theme in part one of the chapter; therefore, to avoid repetition, I will not include it again here.

4.6.3 Working with evidence and guidelines

Interpretation of the humidity literature by clinicians was variable. Some participants stated they were satisfied with current humidification practices and the level of evidence to inform decisions while others reported they were not. While this variability reflects the lack of clear evidence to inform practice, other possibilities exist. One possible explanation for the difference in perceptions is that, in the majority of centres, humidity had been a standard of care for many years and perhaps clinicians have questioned its efficacy less than more recently introduced interventions. Clinicians may make assumptions that existing interventions are safe. To challenge such assumptions implies that routine practices may be harmful. Such challenges are confronting for individuals; it may be safer or easier to maintain the status quo. Another explanation for variable guideline use is that individuals may be reluctant to relinquish control of decision making or perhaps they are critical of recommendations that they perceive as stifling innovation, autonomy and individuality. Alternatively, perhaps it is just that the recommendations within the guidelines mean different things to different people or
groups in different clinical contexts. However, inconsistent practice is challenging for everyone and practice based on personal preference that changes on a regular basis makes evaluation of the effectiveness of our interventions impossible.

This variability in clinicians’ use of evidence and CPGs in everyday practice is acknowledged worldwide (Francke et al. 2008; Hayes & Haines 1998; Kendall et al. 2009; McKinlay et al. 2007; Ploeg et al. 2007; Smith 2012; The McDonnell Social Norms Group 2006), as is the variability in the quality of the guidelines produced (Straus & Shepperd 2011). Despite increasing pressure by administrators, policymakers and clinicians to standardise and reduce variation in practice, in reality, CPGs considered a vehicle to achieve this have had modest effect at best (Whitty, Thomas & Grimshaw 2004). An increasing body of literature that describes the advantages and disadvantages of protocol-based care (Clark 2003; Ilott et al. 2010; Ilott et al. 2006; Rycroft-Malone et al. 2008; Rycroft-Malone et al. 2010; Rycroft-Malone et al. 2009; Rycroft-Malone, Morrell & Bick 2004) provides useful insight, but a discussion of these is beyond the scope of this chapter. The major criticism of standardising practice in neonatal care is that it is at odds with the concept of individualised neonatal care; linear interventions might conflict with complex and unpredictable disease patterns in extremely preterm infants.

A qualitative descriptive study conducted by our research team echoed the challenges of guideline use in the NICU. The study used in-depth semi-structured interviews to investigate EBP and CPG use by nurses within one NICU in Australia (Jorgensen, Sinclair & Crisp, unpublished). The study revealed that research evidence was a relatively unimportant factor in nurses’ clinical decision making and that knowledge of an alternative practice or guideline that is associated with improved outcomes did not always result in a behaviour or practice change. In fact, participants described themselves as being resistant to change and described tension with peers as they sought to maintain the status quo. A large body of literature exists that describes the challenges of research utilisation and proposes models and frameworks that might aid the implementation process, but a discussion of these is beyond the scope of this chapter. I will return to this topic in Chapter 7.
4.6.4 Context of practice

The context of the practice environment affected the use of incubator humidity, the quality of communication and posed a threat to patient care. A plethora of literature attests to the influence of the workplace context on research utilisation (Cummings et al. 2010; Cummings et al. 2007; Kitson, Harvey & McCormack 1998; McCormack et al. 2002; Rycroft-Malone et al. 2004; Rycroft-Malone 2008b), nurses’ job satisfaction, motivation and commitment (Aiken et al. 2002; Aiken et al. 2012; Cummings, Hayduk & Estabrooks 2005; Kangas, Kee & McKee-Waddle 1999; Meijers et al. 2006; Rochefort & Clarke 2010) and patient care (Brown & McCormack 2011; Cricco-Lizza 2011; Lake et al. 2012; Stevens et al. 2011). Identified contextual factors that influence research use and patient care include culture, leadership, teamwork and resources (Gifford et al. 2007; Kitson, Harvey & McCormack 1998; McCormack et al. 2002).

This survey confirmed that these factors influenced humidification practices in NICUs; participants highlighted the challenges of the workplace culture, lack of leadership, barriers to effective teamwork and limited resources. Findings are discussed under the identified subheadings of inconsistencies in practice, individuals and their relationships and staffing and skill mix.

4.6.4.1 Inconsistencies in practice

Several factors contributed to the inconsistencies in humidification practices, both across and within NICUs. These factors included a lack of research evidence, variability in the interpretation of the evidence that does exist, variability in the use of CPGs and the factor having the most influence on practice within NICUs: the varying individual clinician beliefs about the benefits and risks of humidity use. Golec (2009, p. 600) discusses reasons for inconsistencies in practice within NICUs and describes moral distress as an outcome:

> Personal preference, thinly disguised as the ‘art of medicine’, often takes precedence, resulting in an inconsistency of care that can cause a great deal of moral distress for the team, not to mention the detrimental effect it may have on patient care […] It is time that the needs of our tiny patients take priority over the individual artistic approach of any given caregiver.

Hefferman and Heilig (1999) described moral distress as a combination of a sense of great responsibility for infants and families, a feeling of powerlessness to make
treatment decisions and an inability to take action. Moral distress can have important consequences for nurses, including stress, burnout, job dissatisfaction, departure from the work environment and adverse effects on psychological and physical wellbeing, self-image, spirituality (Corley 2002; Corley et al. 2001; Elpem, Covert & Kleinpell 2005; Jameton 1993; Pauly et al. 2009; Schluter et al. 2008) and patient care (Hardingham 2004; Rodney 1988). More research is required to reduce moral distress in the workplace. In the interim, it is essential that neonatal clinicians find ways to achieve local consensus on humidification practices to reduce inconsistencies to improve the practice environment, keep clinicians safe and provide care based on the best available evidence.

4.6.4.2 Individuals and their relationships

Close proximity and the intensity of the work within the NICU places great emphasis on communication and teamwork. Baker, Day and Salas (2006) summarised requirements for successful teamwork that included team leadership, mutual performance, backup behaviour, adaptability, shared mental models, closed loop communication and a collective orientation. In contrast to this ideal, however, this survey found evidence of hierarchical structures with autocratic leadership in which individuals appeared to exert influence over others within many of the NICUs. In these environments, such structures inhibited optimal doctor–nurse and nurse–family relationships that are essential to the provision of quality care. Interpersonal relationships (Bucknall 2003; McVicar 2003) and lack of influence (Silen et al. 2008) are known stressors in critical care work. I argue that neither nursing nor medical education prepares clinicians for interdisciplinary relationships and effective communication, especially in complex, highly stressful environments such as the NICU, and suggest it be included in future curricula. If communication influences clinical quality, patients’ safety, clinicians’ wellbeing and public satisfaction (Iedema 2009), I suggest we seek measures to improve interpersonal relationships as a matter of urgency: ‘Uncontrolled dominance is no longer ethically and scientifically acceptable’ (Liberati & Vineis 2004, p. 120).
4.6.4.3 Staffing and skill mix

Nurse staffing and skill mix affected clinical practice. This finding is consistent with literature that continues to describe the deleterious effects of poor staffing levels and a depleted skill mix on nurse stress and patient outcomes (Aiken et al. 2002; Duffield et al. 2007; Needleman et al. 2011; Twigg et al. 2012), and it underpins nurses’ decisions to leave, or plan to leave, the workforce (Braithwaite 2008; Fischer et al. 2000; Forsyth & McKenzie 2006; Healy & McKay 2000; McGrath, Reid & Boore 2003; McVicar 2003; Silén et al. 2008).

4.7 Chapter Summary

This chapter has presented the first survey of incubator humidification practices in NICUs across Australia and New Zealand. The survey clearly highlighted the diversity in practice both within and between NICUs and supported the hypothesis that there would be wide variation in the practical application of humidity. The variability in practice reflected not only the paucity of rigorous research to guide decision making but also variations in the interpretation of existing evidence and individuals’ views and beliefs, often independent of existing CPGs. The survey revealed how the NICU context influenced humidity use; the multiple factors that were simultaneously at play were explicit throughout. Although there is reasonable biological plausibility that incubator humidity should benefit extremely preterm infants, there is so much variability in its application that it is difficult to determine whether it has any effect or not. What was clear from discussion with the neonatal nurses was that the uncertainty in the practice environment negatively affected not only humidification practices but also the nurses themselves and patient care.

The overwhelming message from this survey is that clinicians need guidance regarding humidity use; making practice decisions without robust evidence is difficult. Nurses described strong perspectives, much frustration and revealed humidity use to be a very emotive subject. The nurses also expressed willingness to contribute to a trial that investigates the benefits and risks of humidity, even if, for some, it would challenge their beliefs about a practice they assumed benign. The survey results illustrated that
what is required is to establish new knowledge to guide clinicians and optimise the delivery of humidity in the management of preterm infants. Specifically, optimal levels and duration of humidification need to be defined and future trials need to be powered to detect clinically important differences in long-term neurodevelopmental and behavioural outcomes. The survey also revealed another covariate, the context of the practice environment.

The survey provided me with the opportunity to develop relationships and network with peers across NICUs. I hoped this might prove advantageous when planning and orchestrating the proposed study. Further, knowledge of local practices and nurses’ views on, and experiences of, humidity as well as factors that would limit or enhance the likelihood that a clinical trial would be acceptable may also prove invaluable.

From the results of this survey, it seems that the human factor had the greatest effect. The showmanship of various personalities continues to drive the adoption of humidification practices (or not) as described in the evolution of the humidified incubator presented in Chapter 2. The survey highlighted the challenges of personality-driven practices. It is unlikely that the generation and dissemination of new guidelines will significantly improve neonatal outcomes if we continue to use personality-driven approaches to patient care. Until we can improve the way that clinicians communicate with each other, the way that they work together and the quality of their interactions, and until individuals understand the implications of their behaviour and decision making, neonatal care will never achieve the evidence-based status it so desires.

4.8 Reflections, Learning and Critical Questions

On reflection, I found the telephone interview a very useful method of data collection and do not believe it limited interaction with participants, as some literature has suggested (Novick 2008). Perhaps I found this method of data collection useful because I took time to identify the nurses within each centre who were positioned best to discuss humidity use. I also made contact, established a rapport and allowed time for the participants to reflect on the questions prior to the interview. Further, I believe that being a peer of the participants with in-depth knowledge of humidity use enhanced the
process. The experience afforded me valuable insights into local practices and the lives of senior neonatal nurses across Australia and New Zealand—an experience about which I feel most privileged. The telephone interview provided me with a great networking opportunity, the benefits of which persist today.

The purpose of the survey was to seek the opinions and unique experiences of neonatal nurses (to capture and portray both commonalities and differences), and thus I made every attempt to remain true to the participants’ accounts. However, as a researcher it was essential for me to recognise that I was a part of the social world under study. Throughout the interviews, I considered the concept of reflexivity and reflected on how my actions, values and perceptions could affect the survey and influence both data collection and analyses (Gerrish & Lacey 2006; Parahoo 2006; Parker 1999). As Gibbs (2007, p. 90) reminded me, ‘the qualitative researcher is not an objective, authoritative, politically neutral observer standing outside and above the text’; and ‘the researcher’s knowledge and preconceptions will inevitably influence the identification of themes’ (Joffe & Yardley 2004, p. 58). Therefore, it was important for me to acknowledge the possibility that I would view the participants’ experiences and views of incubator humidity through the lens of my own personal experiences and cognitive biases resulting from preconceived notions. However, the categorising of responses was in reality a very straightforward process based on the questions asked and simply involved a clustering of responses.

Other potential sources of bias existed. I was affiliated with one of the NICUs and six of the participants knew me, although, at that time, not well because I had recently arrived in Australia. I do not believe my knowing a minority of the participants affected data collection or its interpretation, although I am aware of the potential issues involved (McConnell-Henry et al. 2009–10). My in-depth knowledge on the subject matter and terminology had, in this instance, a positive effect on the interviewer–participant relationship. Without knowledge of incubator humidity and neonatal nursing, I would have been unable to gain respect from or lead the discussion with this group of very experienced nurses. Although the participants seemed to be relaxed, open and honest, I do acknowledge that some participants may have chosen not to disclose fully their beliefs and feelings and that what was disclosed may have differed from actual
behaviour. However, I am confident that my position as CNC and peer of the participants meant that we shared common goals and together developed an environment conducive to discussion and information sharing. In fact, several participants stated they were grateful for the opportunity to discuss concerns and vent frustrations during the interview, especially those for whom uncertainty about humidification practices existed locally. The literature reported such a phenomenon previously; Leinicke et al. (2005) described interviewees who were relieved to discuss their fears with interviewers who were external to the organisation.

The results of the survey have implications for the proposed study. Despite concerns about sepsis risk and the inconsistencies in practice, the survey found the majority of participants supported the use of humidity in the management of extremely preterm infants. This implied that equipoise does not exist for the question—humidity versus no humidity. Ethically, no future clinical trial could include a ‘no humidity’ trial arm. In addition, participants’ responses suggested that many clinicians were convinced of the superiority of high-level incubator humidity (as high as it was possible to provide) in the first weeks of life, for the most immature infants. It could be construed that it may prove difficult to convince clinicians to use a lower level of humidity as part of an RCT.

I still sought further information that was essential in the design of the trial protocol. The introduction of incubator humidity as a standard of care within my workplace presented an opportunity to conduct an audit that compared two cohorts of extremely preterm infants (pre and post introduction of humidity). While acknowledging its limitations, retrospective nature and the need for caution in its interpretation, I believed the audit might serve a useful purpose. This was a unique opportunity because this was the last NICU in NSW to introduce humidity and it enabled the comparison of a group of infants who received humidity with a group of infants who did not. I hoped the audit might help answer some outstanding questions. Which variables are important when investigating the effect of incubator humidity on extremely preterm infants? Can the audit provide information about the distribution of infant characteristics as well as the covariates and outcomes that could inform the sample size? Further, I hoped that the audit might provide additional insight into the practice environment and CPG use as
well as identify feasibility issues for the proposed trial. The following chapter presents and discusses the findings of this single-centre audit.
Chapter 5: C’ing the *Fog of Vapour*:
Complexity of Intervention = Outcome Links

*Retrospective Audit of Humidification Practices*

5.1 Chapter Overview

The work of the thesis so far has exposed the complexity surrounding incubator humidity practices in NICUs. The lack of robust evidence, the variability in the use of CPGs and in clinician opinion on the benefits and risks of humidity use, the consequent inconsistencies in practice and the uncertainty this creates revealed the messiness of the practice environment and left questions for the proposed trial about sample size and outcome variables of relevance unanswered. In an attempt to gain further information and answer these questions, this chapter now presents a single-centre audit of patient medical records that used the opportunity of a recent introduction of incubator humidity as a standard of care within my workplace. The audit compared a group of infants nursed in humidified incubators with a previous cohort of infants cared for in non-humidified incubators (before the practice change).

The audit had three main aims. The first of these was to determine whether patterns existed between the introduction of incubator humidity and the perceived benefits and risks of use and short-term neonatal health outcomes (until hospital discharge). The second aim was to gather information about the distribution of infant characteristics across a range of variables of potential relevance to the processes and outcomes of humidity use that could inform sample size. Knowledge and understanding of the major patterns among these variables would ensure that the trial has sufficient power to test the potential benefits and risks of humidification for this infant population. The third and final aim of the audit was to compare current humidity practices with those detailed within the local CPG to determine, when possible, to what extent the NICU context influenced humidification practices.
5.2 Rationale

The rationale for choosing this NICU for conducting the present audit was a practical one based on several factors. The NICU was my place of employment during the time of the audit, my role as CNC enabled me to access patient medical records, and I had in-depth knowledge of the local context and the CPG. In addition, and most importantly, the provision of incubator humidity was a recently introduced intervention. Recent introduction of incubator humidity as a standard of care provided a timely and unique opportunity to examine local practices and compare two independent groups of extremely preterm infants before and after its introduction. Given that we have previously established that all other NICUs in Australia and New Zealand routinely provide incubator humidity and the majority have done so for many years (Sinclair, Crisp & Sinn 2009), it was apparent that the recent introduction of humidity in this particular NICU afforded the best opportunity to observe possible relationships between humidification and health outcomes.

Knowledge of the local CPG was essential to the audit because one of the aims was to determine the extent to which humidification practices reflected the content within. I have summarised below the recommendations within the CPG that are relevant to this audit:

1. Provide high-level humidity (80%) for all infants less than or equal to 28 weeks gestation at birth.
2. Commence weaning after 72 hours:
   a. Reduce level of humidity by 0.5 °C every 12 hours until 50% is reached.
   b. Increase incubator temperature to maintain the body temperature within normal range during the weaning process.
3. Cease humidity on day seven of life.

5.3 Methods

5.3.1 Design

This chapter used retrospective review methodology. Retrospective studies use existing data that clinicians originally collected for reasons other than research. These historical
medical records contain a wealth of clinically relevant and accessible data that clinicians and researchers have used to inform hypotheses tested in prospective studies (Hess 2004; Jansen et al. 2005), epidemiological investigations (Jansen et al. 2005; Preen et al. 2004; Reid, Dickinson & Doherty 2003), safety and quality assurance projects (Allison et al. 2000; Grasso et al. 2003; Travaglia & Debono 2009), professional education and training (Pan et al. 2005) and evaluation of patient care (Blandthorn, Forster & Love 2011; Murray et al. 2002; Nicoll et al. 2004).

The retrospective audit had several advantages. Since the intention was to gather as much information as quickly as possible about potential relationships between humidification and neonatal outcomes to inform the ongoing work of the thesis, a retrospective audit enabled immediate access to and observation of an existing, rich and readily available data collection. In addition, the inclusion of the progress notes in which clinicians document events contemporaneously enabled the data collected to be as comprehensively as possible. Another advantage of the audit process was that it allowed the review of a considerable number of medical records both before and after implementation of incubator humidity.

It was important also to acknowledge the limitations of retrospective reviews; they are less robust than studies that adopt a prospective approach (Hess 2004; Pan et al. 2005; vonKoss Krowchuk, Moore & Richardson 1995). Limitations included reliance on routinely collected data of paper medical records and documented events, incomplete documentation, variability in the quality of documented information, inability to verify data, possibility of confounding variables and the inability to establish cause and effect. A major potential disadvantage of using audit groups from two different periods was the absence of control over differences in patient population or clinical management between the two periods, which could confound the relationship between humidity exposure and outcomes in unpredictable ways. However, while acknowledging that retrospective audits may be misleading in terms of evidence, for the purpose of this work, it was thought that the audit might provide some insight into the effect of the introduction of incubator humidity as a new therapeutic intervention and, therefore, be potentially useful and worth investing in.
The inclusion criterion consisted of all infants born less than or equal to 28 weeks gestation at birth that survived and received incubator humidity in the NICU. I was unsure initially whether to include ex-utero transfers, that is, extremely preterm infants who were born outside of the tertiary centre. The rationale for my thinking was that birth in a non-tertiary centre followed by postnatal transfer delays initiation of intensive care interventions (including incubator humidity) and has a substantial effect on mortality and morbidity in this infant population (Abdel-Latif et al. 2006; Araujo et al. 2011; Lasswell 2010; Lasswell et al. 2010). However, I decided to include all infants who received incubator humidity following admission to the NICU because this is representative of the extremely preterm infant population in all NICUs.

5.3.2 Setting and sample

A 44-bed NICU in a major tertiary hospital that recently introduced incubator humidity as a standard of care for extremely preterm infants provided the ideal setting for the purposes of audit. Neonatal nurses in this NICU care for infants who are sick, preterm or have congenital anomalies; the majority of infants are preterm. Additionally, nurses support stressed and extremely anxious parents and their extended families through what is commonly termed the roller-coaster ride that is neonatal intensive care. A large multidisciplinary team communicates to provide continuous care: six neonatologists, 120 nurses, fellows, registrars, social workers, home care team, lactation specialists, pharmacists, occupational therapists, speech pathologists, dieticians and specialist physicians when consultations are required.

An electronic search of the NSW and Australian Capital Territory (ACT) Neonatal Intensive Care Units (NICUS) database with assistance from the local data manager identified a sample of extremely preterm infants less than or equal to 28 weeks gestation born consecutively between December 2002 and November 2005 and admitted to the NICU. Auditing this period captured infants born 18 months before and after the introduction of incubator humidity as a standard of care in June 2004. I chose this period for practical reasons, incubator humidity commenced 18 months prior to the commencement of the audit; I included the only data available. I was confident this would at least ensure that the rough rule for determining sample size that would ensure
data were clinically useful (10 records per variable) (Sackett et al. 1991) was achieved. The audit compared demographic and clinical data of the two cohorts of extremely preterm infants. The work in Chapters 2, 3 and 4, discussions with neonatologists and specific aspects within the local CPG informed the choice of variables used to populate a database for the purpose of data collection.

5.3.3 Ethical considerations

Ethical considerations relevant to this survey related to issues of privacy, confidentiality and data storage. The relevant university (2005-163) and health service (2005/8/6.1(2173)) scientific and HRECs approved the conduct of the audit. Although risk is present in all research, the risks to participants were minimal because this was a retrospective audit. I stored the data in secure cabinets and on password-protected computer files in my office; only I had access to the data files to ensure maximum privacy. To protect confidentiality, a separate filing cabinet maintained the security of patient medical record numbers (MRNs) that identified individual infants. I removed the MRNs following data entry to ensure that records did not contain potentially identifying information. The SPSS database contained only de-identified data. Since seven years have now passed, I destroyed all survey data in accordance with the NHMRC’s National Statement on Ethical Conduct in Research Involving Humans (NHMRC 2007).

5.3.4 Data collection

I collected the data between October 2005 and January 2006. The data collected included a number of potential variables and outcome measures of relevance to incubator humidity use from the medical records of infants born in the 18 months before and after introduction of humidity. I developed continuous variables for each of the physiological parameters that might reflect the effect of a humidified environment, including body temperature, daily fluid requirements, serum sodium and potassium levels, and weight loss or gain. Variables that assessed incidence of the potential risks of humidity use included episodes of hyperthermia, culture positive sepsis and gram-negative colonisation of any site. Assessment of skin integrity requires an Evaporimeter that measures TEWL. Clinicians in NICUs rarely use Evaporimeters outside of a clinical trial; therefore, skin integrity is one parameter that could not be included in this
audit. According to the CPG within the NICU, infants less than or equal to 28 weeks gestation received incubator humidity in the first seven days of life. Data collection covered the same period.

I retrieved the data from several sources. The demographic data collected from the NICUS database included date of birth, gestational age, gender, Apgar scores at one and five minutes of age, birth weight and percentile for gestational age. I included two early therapeutic interventions that influence health outcomes: maternal antenatal steroids and exogenous surfactant administration. Chart reviews determined fluid intake, weight loss or gain and body temperature. Access to the electronic health record charting system provided pathology (serum sodium and potassium), microbiology (culture) and radiology (cranial ultrasound). Although it might have been useful to collect data on phototherapy use, review of the nursing notes revealed that nurses did not document initiation and cessation of phototherapy consistently; therefore, I could not include this as a variable.

No core outcome sets for extremely preterm infants exist. However, I included the following outcome variables because they are valid, reproducible, relevant to the extremely preterm infant population, used to assess the effect of other NICU interventions and responsive to changes in thermoregulation and fluid balance: PDA, CLD, IVH, NEC and mortality. The NICU admission books and documentation from the mortality review group confirmed information about neonatal mortality.

As highlighted in the survey of humidification practices (Chapter 4), the context of the practice environment is an additional covariate that has the potential to complicate the design and execution of a future trial. Variables that measured humidification practices in the NICU included the level of humidity, duration of use and the weaning process. Review of both the charts and progress notes explored, when possible, evidence of decision making about humidity use. The local data manager confirmed the accuracy and completeness of the dataset.
5.4 Analyses

All data were analysed using SPSS Version 15 (SPSS Inc., Chicago, IL, USA). Since body temperatures can vary between measurements, the means (median) of all daily body temperatures were compared. Other continuous measures summarised as means were compared using the independent samples t-test. Chi-square testing was used for categorical data as appropriate to test for associations between humidity use and short-term health outcomes. Valid percentages are reported throughout. Logistic regression analysis was used to factor out variance associated with group differences. For all analyses, p-values < 0.05 were considered statistically significant.

5.5 Results

The NICUS database search identified 230 infants less than or equal to 28 weeks gestation born between June 2004 and December 2005. Retrieval and review of the medical records showed that 19 of the infants either did not receive humidity (n = 11) or received humidity for only a few hours (n = 8) following implementation of the guideline and were thus excluded. Therefore, 211 infants were eligible for inclusion in the audit. The audit then compared pre- and post-intervention data from two cohorts of infants: 109 infants who received incubator humidity as part of routine care compared with 102 infants who did not receive humidity.

Table 3 presents patient demographics and early therapeutic interventions for infants in both study groups. The group of infants who received humidity were of lower gestational age, birth weight and percentile for gestational age than the group of infants that did not receive humidity. This disparity between the two groups is further emphasised in Figures 2 to 5, which visibly depict the difference in the distribution of infants in relation to gestational age and birth weight between the two groups. Figures 2 to 3 demonstrate the differences in gestational age between the audit groups, and Figures 4 to 5 show the differences in birth weight between the two groups. Analysis revealed no statistical difference between the groups in relation to gender or early therapeutic interventions (the number of doses of surfactant administered and administration of maternal antenatal steroids). Although more mothers of infants in the
humidity group did not receive a complete course of antenatal steroids (57 mothers compared with 47 in the non-humidity group), this did not reach statistical significance ($p < 0.051$).

**Table 3: Patient Demographics and Early Therapeutic Interventions**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Humidity n = 102</th>
<th>Humidity n = 109</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>27.5 (1.4)</td>
<td>26.0 (1.4)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>225.4 (285.7)</td>
<td>155.1 (285.7)</td>
</tr>
<tr>
<td>MD (CI)</td>
<td>1.5 (1.09–1.83)</td>
<td>225.4 (1.09–1.83)</td>
</tr>
<tr>
<td>t* df p</td>
<td>7.8 209 &lt;0.0001</td>
<td>7.8 209 &lt;0.0001</td>
</tr>
</tbody>
</table>

**Table 3: Patient Demographics and Early Therapeutic Interventions**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Humidity n = 102</th>
<th>Humidity n = 109</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (grams)</td>
<td>1092 (258)</td>
<td>867 (174)</td>
</tr>
<tr>
<td>Percentile</td>
<td>54 (28.5)</td>
<td>45 (26.1)</td>
</tr>
<tr>
<td>Gender: Male</td>
<td>48 (47%)</td>
<td>50 (46%)</td>
</tr>
<tr>
<td>Female</td>
<td>54 (53%)</td>
<td>59 (54%)</td>
</tr>
<tr>
<td>Received antenatal steroids</td>
<td>84 (82%)</td>
<td>85 (78%)</td>
</tr>
<tr>
<td>Received complete steroid course</td>
<td>54 (53%)</td>
<td>43 (39%)</td>
</tr>
<tr>
<td>Received surfactant</td>
<td>73 (72%)</td>
<td>89 (82%)</td>
</tr>
</tbody>
</table>

* $t*$ = Student’s t-test for independent groups

**Figure 2: Gestational Age No Humidity**
Table 4 shows daily mean humidity levels provided for the 109 infants in the post-intervention group. No infant received humidity beyond seven days of life. Of the 109 infants who received humidity, 27 infants did not receive humidity for the full seven completed days as per the guideline recommendations. Results revealed a wide variation
in the range of humidity levels provided on a daily basis (for example 40–96% on day one of life when target was 80%). Documentation within the progress notes confirmed that the practice variation often occurred as a direct result of individual clinicians (predominately consultants, occasionally senior nurses who were in team leader and management roles) ceasing humidity when they assumed care of the infant.

**Table 4: Level of Incubator Humidity (%) Provided in First 7 Days of Life**

<table>
<thead>
<tr>
<th>Day</th>
<th>Mean (%)</th>
<th>Min/Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>79</td>
<td>(40–96)</td>
</tr>
<tr>
<td>2</td>
<td>78</td>
<td>(45–92)</td>
</tr>
<tr>
<td>3</td>
<td>77</td>
<td>(47–93)</td>
</tr>
<tr>
<td>4</td>
<td>73</td>
<td>(43–92)</td>
</tr>
<tr>
<td>5</td>
<td>65</td>
<td>(40–87)</td>
</tr>
<tr>
<td>6</td>
<td>57</td>
<td>(30–86)</td>
</tr>
<tr>
<td>7</td>
<td>53</td>
<td>(40–83)</td>
</tr>
</tbody>
</table>

Table 5 displays mean fluid requirements, serum sodium and potassium levels and weight loss in the first week of life. The results illustrate a statistically significant increase in fluid requirements on days three to seven of life in infants who did not receive humidity compared with the infants who did receive humidity. Infants in the humidity group had higher mean potassium levels on day four (p < 0.001) and day five (p < 0.048) of life. However, there was no difference in mean sodium levels or incidence of hypernatraemia between the two groups. Infants who did not receive humidity experienced greater weight loss (p < 0.045). Variations in the degrees of freedom reflect mortality and differences in clinical need for ongoing investigations.
Table 5: Mean Fluid Requirements, Serum Sodium and Potassium Levels and Weight Loss in the First Week of Life

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Humidity n = 102</th>
<th>Humidity n = 109</th>
<th>MD (CI)</th>
<th>t* df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluids(^a)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>84.0 (12.3)</td>
<td>81.7 (20.1)</td>
<td>2.3 (−2.31–6.86)</td>
<td>0.97</td>
<td>208</td>
</tr>
<tr>
<td>Day 2</td>
<td>95.9 (21.2)</td>
<td>91.1 (24.5)</td>
<td>4.8 (−1.49–11.02)</td>
<td>1.50</td>
<td>208</td>
</tr>
<tr>
<td>Day 3</td>
<td>115.4 (29.9)</td>
<td>106.0 (23.6)</td>
<td>9.4 (−1.98–16.83)</td>
<td>2.49</td>
<td>201</td>
</tr>
<tr>
<td>Day 4</td>
<td>125.7 (29.9)</td>
<td>115.3 (22.5)</td>
<td>10.3 (3.03–17.71)</td>
<td>2.78</td>
<td>199</td>
</tr>
<tr>
<td>Day 5</td>
<td>127.4 (22.0)</td>
<td>117.8 (21.9)</td>
<td>9.6 (3.45–15.80)</td>
<td>3.08</td>
<td>195</td>
</tr>
<tr>
<td>Day 6</td>
<td>129.8 (19.6)</td>
<td>118.3 (18.0)</td>
<td>11.4 (6.13–16.75)</td>
<td>4.25</td>
<td>194</td>
</tr>
<tr>
<td>Day 7</td>
<td>131.3 (17.7)</td>
<td>120.4 (18.9)</td>
<td>10.8 (5.62–16.03)</td>
<td>4.10</td>
<td>191</td>
</tr>
<tr>
<td>Serum sodium(^b)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>138.4 (4.5)</td>
<td>137.9 (4.8)</td>
<td>0.59 (−0.69–1.87)</td>
<td>0.91</td>
<td>206</td>
</tr>
<tr>
<td>Day 2</td>
<td>143.7 (5.1)</td>
<td>143.0 (5.4)</td>
<td>0.77 (−0.68–2.23)</td>
<td>1.05</td>
<td>204</td>
</tr>
<tr>
<td>Day 3</td>
<td>144.1 (4.6)</td>
<td>144.5 (5.1)</td>
<td>−0.44 (−1.79–0.91)</td>
<td>−0.64</td>
<td>200</td>
</tr>
<tr>
<td>Day 4</td>
<td>141.2 (4.0)</td>
<td>142.1 (4.3)</td>
<td>−0.91 (−2.07–0.24)</td>
<td>−1.56</td>
<td>198</td>
</tr>
<tr>
<td>Day 5</td>
<td>138.6 (3.6)</td>
<td>139.4 (3.7)</td>
<td>−0.80 (−1.84–0.24)</td>
<td>−1.52</td>
<td>195</td>
</tr>
<tr>
<td>Day 6</td>
<td>137.3 (4.0)</td>
<td>137.8 (3.8)</td>
<td>−0.52 (−1.62–0.58)</td>
<td>−0.93</td>
<td>191</td>
</tr>
<tr>
<td>Day 7</td>
<td>136.6 (3.7)</td>
<td>137.0 (3.9)</td>
<td>−0.37 (−1.45–0.71)</td>
<td>−0.68</td>
<td>189</td>
</tr>
<tr>
<td>Serum potassium(^c)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>5.34 (0.96)</td>
<td>5.47 (0.89)</td>
<td>−0.13 (−0.38–0.13)</td>
<td>−0.97</td>
<td>206</td>
</tr>
<tr>
<td>Day 2</td>
<td>4.76 (0.92)</td>
<td>4.99 (0.98)</td>
<td>−0.23 (−0.49–0.33)</td>
<td>−1.72</td>
<td>201</td>
</tr>
<tr>
<td>Day 3</td>
<td>4.64 (0.85)</td>
<td>4.62 (0.90)</td>
<td>0.02 (−0.23–0.26)</td>
<td>0.14</td>
<td>199</td>
</tr>
<tr>
<td>Day 4</td>
<td>4.93 (0.88)</td>
<td>4.53 (0.75)</td>
<td>0.41 (0.18–0.64)</td>
<td>3.48</td>
<td>192</td>
</tr>
<tr>
<td>Day 5</td>
<td>5.05 (0.90)</td>
<td>4.80 (0.81)</td>
<td>0.25 (0.00–0.49)</td>
<td>1.99</td>
<td>188</td>
</tr>
<tr>
<td>Day 6</td>
<td>5.14 (0.90)</td>
<td>5.06 (0.90)</td>
<td>0.08 (−0.18–0.34)</td>
<td>0.60</td>
<td>185</td>
</tr>
<tr>
<td>Day 7</td>
<td>5.04 (0.85)</td>
<td>5.06 (0.87)</td>
<td>−0.02 (−0.27–0.23)</td>
<td>−0.14</td>
<td>180</td>
</tr>
</tbody>
</table>

7 day weight loss (grams) 127.0 (72.7) 108.0 (58.3) 19.0 (0.41–37.63) 2.03 195 <0.045

\*t = Student’s t-test for independent groups \(^a\)mL/Kg/day \(^b\)mmol/L

Table 6 reflects thermoregulatory state. Infants in the humidity group experienced more episodes of hypothermia (p < 0.007) than those in non-humidified group on day three of life. There was also a statistically significant increased risk of hyperthermia on day 1 (p < 0.001) and day 4 (p < 0.007) of life for infants in the humidity group.
Table 6: Number of Episodes of Hypothermia (<36.0 °C) and Hyperthermia (>37.5 °C) in First Week of Life

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Humidity n = 102</th>
<th>Humidity n = 109</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Episodes of hypothermia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>0.43 (0.8)</td>
<td>0.37 (0.6)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 2</td>
<td>0.10 (0.3)</td>
<td>0.06 (0.2)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 3</td>
<td>0.14 (0.4)</td>
<td>0.03 (0.2)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 4</td>
<td>0.12 (0.4)</td>
<td>0.11 (0.3)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 5</td>
<td>0.11 (0.3)</td>
<td>0.06 (0.2)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 6</td>
<td>0.06 (0.3)</td>
<td>0.07 (0.3)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 7</td>
<td>0.11 (0.4)</td>
<td>0.03 (0.2)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td><strong>Episodes of hyperthermia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>0.33 (0.7)</td>
<td>0.74 (1.0)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 2</td>
<td>0.20 (0.5)</td>
<td>0.22 (0.5)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 3</td>
<td>0.20 (0.5)</td>
<td>0.17 (0.5)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 4</td>
<td>0.27 (0.6)</td>
<td>0.08 (0.3)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 5</td>
<td>0.20 (0.6)</td>
<td>0.13 (0.4)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 6</td>
<td>0.16 (0.4)</td>
<td>0.09 (0.3)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Day 7</td>
<td>0.20 (0.5)</td>
<td>0.08 (0.3)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
</tbody>
</table>

Table 7 presents the outcome variables potentially affected by humidity use in relation to infants in both groups. Analysis revealed that the group of infants who received humidity had a statistically significant increase in mortality (p < 0.020), PDA (p < 0.0001), CLD (p < 0.004) and gram-negative colonisation (p < 0.019). There was no observed difference in the incidence of culture positive sepsis, IVH or NEC between the two groups.
Table 7: Short-Term Neonatal Health Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Humidity (n = 102)</th>
<th>Humidity (n = 109)</th>
<th>Relative Effect</th>
<th>Absolute Effect</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>5 (5)</td>
<td>16 (15)</td>
<td>2.99 (1.14–7.88)</td>
<td>0.10 (0.02–0.18)</td>
<td>&lt;0.020</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>33 (32)</td>
<td>63 (58)</td>
<td>1.79 (1.29–2.47)</td>
<td>0.25 (0.12–0.38)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Culture positive sepsis</td>
<td>2 (2)</td>
<td>11 (10)</td>
<td>5.15 (1.17–22.66)</td>
<td>0.08 (0.02–0.14)</td>
<td>&lt;0.094</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>22 (24)</td>
<td>44 (43)</td>
<td>1.75 (1.14–2.68)</td>
<td>0.17 (0.05–0.29)</td>
<td>&lt;0.004</td>
</tr>
<tr>
<td>IVH (any grade)</td>
<td>29 (28)</td>
<td>37 (34)</td>
<td>1.19 (0.80–1.79)</td>
<td>0.06 (–0.07–0.18)</td>
<td>&lt;0.286</td>
</tr>
<tr>
<td>IVH (grades 3&amp;4)</td>
<td>7 (7)</td>
<td>14 (13)</td>
<td>1.87 (0.79–4.45)</td>
<td>0.06 (0.05–0.29)</td>
<td>&lt;0.160</td>
</tr>
<tr>
<td>Necrotising enterocolitis</td>
<td>11 (48)</td>
<td>12 (52)</td>
<td>1.02 (0.47–2.21)</td>
<td>0.00 (–0.08–2.21)</td>
<td>&lt;1.000</td>
</tr>
<tr>
<td>Gram-negative colonisation</td>
<td>9 (9)</td>
<td>20 (18)</td>
<td>2.08 (0.99–4.35)</td>
<td>0.10 (0.00–0.19)</td>
<td>&lt;0.019</td>
</tr>
</tbody>
</table>

Logistic regression analysis estimated the effect of humidity versus no humidity on statistically significant binary outcome variables (PDA, CLD and mortality), taking into account other confounding variables that might affect the outcome (gestational age and birth weight). Table 8 shows the analysis and reveals that gestational age and to a lesser extent birth weight, not humidity use, was predictive of short-term health outcomes.

Table 8: Logistic Regression: Incubator Humidity and Short-Term Outcomes

| Classification Tablea |
|-----------------------|---------------------|------------------|-----------------|-----------------|-----------|
| Observed              | Predicted           |                   | Received incubator humidity or not | Percentage Correct |
|                       |                     |                  | no humidity     | humidity        |           |
|                       |                     |                  | 69              | 32              | 68.3      |
| Step 1                | Received incubator  | 27               | 83              |                | 75.5      |
|                       | humidity or not     |                  |                 |                |           |
| Overall Percentage    |                      |                  |                 |                | 72.0      |

a. The cut value is .500
### Variables in the equation

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>S.E.</th>
<th>Wald</th>
<th>df</th>
<th>Sig</th>
<th>Exp(B)</th>
<th>95% C.I. for EXP(B)</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brthwgt</td>
<td>-.003</td>
<td>.001</td>
<td>6.409</td>
<td>1</td>
<td>.011</td>
<td>.997</td>
<td>.995 .999</td>
<td></td>
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</tr>
<tr>
<td>Gestn</td>
<td>-.472</td>
<td>.172</td>
<td>7.568</td>
<td>1</td>
<td>.006</td>
<td>.624</td>
<td>.445 .873</td>
<td></td>
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</tr>
<tr>
<td>PDA</td>
<td>.202</td>
<td>.350</td>
<td>1.331</td>
<td>1</td>
<td>.565</td>
<td>1.223</td>
<td>.616 2.431</td>
<td></td>
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</tr>
<tr>
<td>Step 1* CLD</td>
<td>-.269</td>
<td>.410</td>
<td>.431</td>
<td>1</td>
<td>.511</td>
<td>.764</td>
<td>.342 1.706</td>
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</tr>
<tr>
<td>Mortality</td>
<td>.090</td>
<td>.667</td>
<td>.018</td>
<td>1</td>
<td>.893</td>
<td>1.094</td>
<td>.296 4.039</td>
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<td></td>
</tr>
<tr>
<td>Neg_site</td>
<td>.801</td>
<td>.539</td>
<td>2.204</td>
<td>1</td>
<td>.138</td>
<td>2.227</td>
<td>.774 6.411</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>15.113</td>
<td>4.354</td>
<td>12.049</td>
<td>1</td>
<td>.001</td>
<td>3658995.247</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a. Variable(s) entered on step 1: Brthwgt, Gestn, PDA, CLD, Mortality, Neg_site.*

### 5.6 Discussion

This single-centre retrospective audit of patient medical records compared data from two groups of infants less than or equal to 28 weeks gestation at birth. The audit compared one group of infants who, following practice change and the implementation of a CPG, received incubator humidity for the first seven days of life with a second group of infants born prior to the introduction of humidity as a standard of care. I will now discuss the audit findings under the following headings of interest, *patient population, humidification practices and use of the CPG and outcome variables of relevance.*

#### 5.6.1 Patient population

Disappointingly, analysis of the data revealed two non-comparable infant groups. Results from descriptive statistics demonstrated that the group of infants who received incubator humidity following its introduction as a standard of care were smaller and more preterm than the group of infants who did not. What is clear from this audit is that the larger number of more preterm infants reported in the second cohort reflects a predicted epidemiologic shift; improved antenatal, perinatal and neonatal care practices means admission to a NICU even for the most immature infants is increasingly a
realistic outcome. The ‘NSW Mothers and Babies Report’ (NSW Department of Health 2007) reported an increasing birth rate and, therefore, an increasing preterm birth rate during the period of audit. In addition, the Australia and New Zealand Neonatal Network (ANZNN) 2006 Annual Report stated that this particular NICU had provided care for the highest number of extremely preterm infants when compared with other NICUs within the audit period (ANZNN 2009). These factors may explain the difference between the two study populations over time. As the two groups of infants are essentially different, the audit cannot attribute the results observed to humidity use.

The audit found no major differences between the groups in relation to gender or early therapeutic interventions (antenatal steroid use and surfactant administration). However, mothers of infants in the humidity group were more likely to have received an incomplete course of antenatal steroids than those in the non-humidified group. As the infants who received humidity were more immature, this finding may simply reflect the urgency and precipitate nature of extremely preterm birth that allows no time to complete the course. A complete course of steroids is necessary to maximise the therapeutic effect; therefore, the incomplete dosing observed in the infants in the humidity group is likely to have contributed to the extent of respiratory distress and influenced associated outcomes (Roberts & Dalziel 2006).

### 5.6.2 Humidification practices and use of the CPG

The results revealed wide variation in the range of humidity levels provided to preterm infants. Although mean humidity levels reflected existing guideline recommendations, there was variability in the levels of humidity infants actually received on a daily basis. The reduction in humidity levels over time reflects the weaning process, but again, there was evidence of wide variation in weaning practices. These findings are not surprising given the lack of clear evidence to direct clinical care and the variations in humidification practices across and within NICUs highlighted by this work (Chapter 4).

Care plans changed with clinician handover. While no infant received humidity beyond seven days in accordance with the guideline recommendations, early cessation of humidity occurred in 27 infants. Review of the progress notes captured, when
documented, decision making related to the variability in practices. Changes that were not consistent with the existing guideline occurred in response to shift changes and whether individual clinicians supported humidity use. It was possible to predict occasions when clinician behaviour would influence patient care. These shift-by-shift changes reflect the findings from the survey (Chapter 4). Of interest, the time of day and day of the week also influenced decision making of clinicians; early cessation of humidity commonly occurred on evening, night or weekend shifts, when there are fewer senior clinicians around. Worthy of note also was the significant number of infants who were eligible for inclusion but were excluded because they did not receive humidity. Again, when documented, this primarily indicated individual clinicians’ non-adherence to the recommendations within the CPG and decisions made not to use humidity.

Inconsistencies in care provision challenges practice review. The inconsistencies in humidification practices highlighted in the audit may not have allowed me to observe any meaningful patterns within the data even if the two groups of infants had been homogeneous. The findings provided significant insight into the reality of the clinical environment within this NICU and revealed not only considerable variation in humidification practices, but also vital information that confirms that the context of the practice environment is an additional covariate or factor influencing patient care and the design and conduct of clinical trials and, therefore, merits consideration in future studies.

The results of this audit are congruent with other work. The audit validates previous published work that reports the variability in the use of CPGs in health care (Francke et al. 2008; Grimshaw, Eccles & Tetroe 2004; Grimshaw et al. 2004; Grimshaw et al. 2002; McKinlay et al. 2007; Whitty, Thomas & Grimshaw 2004) and the influence of the context of the practice environment on research utilisation and patient care (McCormack et al. 2002; Rycroft-Malone et al. 2004). Further, the inconsistencies in humidification practices reflect those identified in the survey presented in Chapter 4. Results of a study that interviewed nurses in this NICU conducted by our team (Jorgensen, Sinclair & Crisp, unpublished) adds some insight and a deeper understanding of this NICU context and use of CPGs, and adds clarity to the findings of this audit. The study identified four themes that negatively influenced the working
environment. These themes were lack of respect between nurses, lack of support of EBP by management, lack of autonomy and poor role perception, and tensions between the nursing and medical teams.

5.6.3 Outcome variables of relevance

5.6.3.1 Fluids and electrolytes

The audit demonstrated differences in fluid requirements and electrolyte balance. Infants who did not receive humidity had increased fluid requirements on day’s three to seven of life compared with the infants who did receive humidity. While this is consistent with evidence that suggests humidity reduces TEWL and therefore reduces fluid requirements (Hammarlund et al. 1977; Hammarlund, Sedin & Stromberg 1982b, 1983; Harpin & Rutter 1985; Sedin, Hammarlund & Stromberg 1983b; Takahashi, Hoshi & Nishida 1994), it was interesting to observe that it was true even though the infants in the non-humidified group were larger and more mature and perhaps expected to have reduced fluid losses when compared with more preterm infants. Therefore, it is not surprising that the infants who did not receive humidity experienced greater weight loss. There was no difference in mean sodium levels or incidence of hypernatraemia between the two groups. Infants in the humidity group had higher mean potassium levels on days four and five of life. An increased incidence of non-oliguric hyperkalaemia in infants in the humidity group is likely to reflect the degree of immaturity. The differences in gestational age between the two cohorts help explain this finding.

5.6.3.2 Thermal management

Infants in the humidity group experienced more episodes of hypothermia than those in the non-humidified group on day three of life. This appeared to coincide with commencement of the weaning process, although guideline recommendations suggested weaning after 72 hours of high-level humidity. It is plausible to assume that the corresponding increase in incubator temperature that is required to maintain thermal stability following reduction in the level of humidity did not occur or was inadequate. This complication of humidity use was highlighted by a number of participants in the
survey (Chapter 4) who recommended vigilance in body temperature monitoring at this crucial time because the metabolic cost of heat loss is huge for the most preterm infants.

Infants who received humidity experienced more episodes of hyperthermia on days one and four of life. One possible explanation for an increased incidence of hyperthermia on day one of life is inadequate monitoring and/or control of the environmental temperature following commencement of high-level humidity. An increased incidence of hyperthermia on day four occurred following a statistically significant hypothermia on day three of life. One explanation for this finding is that the increase in incubator temperature in response to hypothermia associated with the weaning of humidity caused overshoot and the resultant hyperthermia. The literature recognises hyperthermia as a risk of humidity use (Harpin & Rutter 1985), and this finding is consistent with the experiences and validates the concerns of participants in the survey of humidification practices. Preventing hyperthermia may be as important as preventing hypothermia in the management of extremely preterm infants. Thermal management is a priority of the neonatal nurse and needs to be included in ongoing education programs.

5.6.3.3 Short-term health outcomes

It was impossible to observe any patterns or draw any conclusions about the possible effect of humidity on outcome variables because the demographics of the two infant groups differ significantly. Therefore, it was not surprising to find that the smaller, more vulnerable preterm infants in the humidity group had a higher incidence of PDA, CLD and death. Although the audit found no increased incidence in culture positive sepsis, an increased incidence of colonisation of gram-negative organisms reached statistical significance. This finding supports previous studies that have reported increased skin colonisation in humidified microenvironments (Harpin & Rutter 1985; Moffet, Allan & Williams 1967) and validates survey participants’ concerns about increased sepsis risk in humidified environments. However, it will require large prospective studies to confirm the potential relationship between sepsis and incubator humidity.

Since conducting this audit, other researchers have conducted a similar audit in Boston, Massachusetts. Kim et al. (2010) published a retrospective study involving 182
extremely low birth weight infants that compared similar cohorts pre and post the introduction of incubator humidity. Infants in the study received 70% to 80% in the first week of life followed by 50% to 60% until 30 to 32 weeks gestation. The paper provided no rationale for the level or duration of humidity chosen. Infants who received humidity had lower fluid requirements, urine output, insensible water loss and weight loss, and a lower incidence of hypernatraemia during the first week of life. Body temperatures were similar in the two groups. The study reported a decreased incidence of severe CLD (defined as oxygen requirement ≥ 30% and/or positive pressure at 36 weeks gestational age) with no difference in sepsis, NEC, IVH and all CLD. The researchers attributed a reduced incidence of severe CLD to the reduction in fluid intake. However, there was no mention of incidence of PDA in either infant group. The incidence of both gram-positive and gram-negative sepsis was higher in the humidity group when compared with the non-humidified group, but the difference was not statistically significant.

5.7 Conclusions

The purpose of the audit was to determine whether patterns existed between the introduction of incubator humidity and short-term neonatal health outcomes, describe the distribution of infants across a range of variables of potential relevance to humidity use and explore the relationship between humidification practices and the recommendations detailed in the local CPG. Since the audit revealed two non-comparable groups that yielded little information about the effect of humidity on neonatal health outcomes, it was not possible to uncover any patterns among practices and outcomes that may inform future research. Equally, the data could provide no meaningful information about the distribution of infants across variables of relevance to humidification. The change in the infant population adds further confounders to the challenges of discerning evidence of effectiveness.

What the audit did reveal was further evidence of the diversity in humidification practices, the variability in the extent to which clinicians used existing guidelines and how contextual factors can influence patient care. These findings highlight the need for strong RCT evidence to inform incubator humidification practices as well as the need to
understand better the multiple contextual factors within the practice environment that are influential in the success or failure of the implementation of guideline implementations and practice change.

5.8 Reflections, Learning and Critical Questions

It was somewhat disappointing that the audit revealed two very different patient groups and, therefore, could not achieve its intended aims. However, what I was learning about the realities of the practice environment through the lens of a researcher was compelling. Similar to the findings of the survey presented in the previous chapter, this audit identified varying opinions and beliefs and a lack of consensus on incubator humidity use that resulted in inconsistencies in practice and failure to comply with local guidelines.

What did this mean for the proposed trial? How do we achieve compliance with a trial protocol given the inconsistencies in practice, failure to comply with existing guidelines and varying views of incubator humidity that has been demonstrated repeatedly throughout this work? Is it important to understand the social climate and dynamics within individual NICUs before conducting a multicentre study if data are to be meaningful? Moreover, how do we embed the complexities within the protocol? Is it possible to do so?

The following chapter presents a protocol for the proposed clinical trial that goes some way to taking complex clinical contexts into account. Further, the chapter explains why conducting the trial was not feasible within the work of the thesis and reveals a change in the focus of the work that prepares the reader for Chapters 7 and 8.
Chapter 6: C’ing the Misty Atmosphere of Speculation:  

The Complexity of Robust Randomised Controlled Trials  

Protocol for a Cluster Randomised Controlled Trial

6.1 Chapter Overview

This chapter is an important one because it was the turning point of the thesis—a turning point in my thinking and of my view of the health care world. At the beginning of the work, I sat comfortably in a realist world and was certain that the best way to assess the efficacy of interventions and standardise care was to conduct an RCT. In support of this view, the current health care environment is demanding evidence-based care and the results of clinical trials to inform decision making. Therefore, it seemed logical to me that what was required to correct the knowledge gap about incubator humidity use was to design and undertake an RCT that compared the effects of varying levels and durations of humidity on clinically important health outcomes. Evaluating the benefits and risks of existing interventions has become increasingly important because there is consistent evidence of no reduction in morbidity in the extremely preterm infant population over time. Incubator humidity has been a routine practice for over 15 years in Australia and New Zealand (Sinclair, Crisp & Sinn 2009), yet we do not know if this intervention influences morbidity and mortality. Although there is a physiological argument to use humidity soon after birth to reduce large transepidermal water and heat losses, no outcome-based evidence exists to direct clinical practice. Inconsistencies in humidification practices are, in part, a consequence of this paucity of evidence.

The chapters thus far have presented the systematic approach taken to achieve the aim of gaining sufficient knowledge and evidence about incubator humidity use in the management of extremely preterm infants to enable me to conduct an RCT and answer longstanding clinical questions that might optimise and standardise humidification practices. This search for certainty included a systematic review of RCTs—considered the highest level of empirical evidence—to see if I could discover evidence of efficacy; but this review provided little to guide clinicians in the use of humidity. Further, as the work of the thesis progressed, each chapter provided insight into the reality of
evaluating existing interventions and the challenges of the RCT methodology, together with my evolving understanding of the influences of complex clinical contexts on interpersonal relationships, knowledge generation and patient care.

My main goal in this current chapter is to present a draft protocol for the proposed RCT and explain why, given my increasing understanding of the complex and dynamic nature of the NICU context and the challenges associated with knowledge generation, it was impossible to proceed with the RCT within the work of the thesis. I present the chapter in two parts. In the first part, I present the protocol for the RCT that suggests what a study that investigates the effect of incubator humidity on neonatal health outcomes might look like. In the second part, I provide a critical analysis of the chosen trial design and the feasibility of a large multicentre trial given the inconsistencies in practice, the complexity of clinical contexts and the individuals involved.

6.2 Study Protocol

The following section presents the study protocol (in PDF format). If we were to conduct a trial to assess the effect of incubator humidity on neonatal health outcomes, given the complexities discussed, this is one option of what such a trial protocol might look like. The protocol presents a CRCT design using the format of the new and recently published 2013 Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Statement. The 2012 Consolidated Standards of Reporting Trials (CONSORT) Statement: Extension to Cluster Randomised Trials also guided the development of the protocol (Campbell et al. 2012; Chan et al. 2013). I will provide a rationale for the choice of study design later in the chapter. The reader will notice that the protocol at times uses a different voice compared with the work of thesis.
**HUMIDITY IN INCUBATORS FOR PRETERM INFANTS (HIPI): A MULTICENTRE CLUSTER RANDOMISED STUDY**

### 2. Trial Registration

<table>
<thead>
<tr>
<th>Data category</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary registry/trial no</td>
<td>Perinatal Trials Registry—PT0541</td>
</tr>
<tr>
<td>Date of registration</td>
<td>2006</td>
</tr>
<tr>
<td>Source(s) of support</td>
<td>To be confirmed</td>
</tr>
<tr>
<td>Primary sponsor</td>
<td>To be confirmed</td>
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<tr>
<td>Contact for scientific/public queries</td>
<td>Lynn Sinclair, Clinical Nurse Consultant Newborn Services, NSW Pregnancy and Newborn Services Network (PNSN), University of Technology, Sydney, Australia</td>
</tr>
<tr>
<td>Public title</td>
<td>Humidity in Incubators for Preterm Infants</td>
</tr>
<tr>
<td>Scientific title</td>
<td><em>Humidity in Incubators for Preterm Infants (HIPI): A Cluster Randomised Study</em></td>
</tr>
<tr>
<td>Countries of recruitment</td>
<td>Australia, New Zealand</td>
</tr>
<tr>
<td>Health condition studied</td>
<td>Incubator humidity use in extremely preterm infants</td>
</tr>
</tbody>
</table>
| Intervention(s)     | Lower (50–70%) versus higher (80–90%) level of humidity and short (14 days) versus long (28 days) duration of humidity. Four comparators: 1. Low level and short duration of humidity  
                       2. Low level and long duration of humidity  
                       3. High level and short duration of humidity  
                       4. High level and long duration of humidity                                                                                           |
| Key inclusion and exclusion criteria | Inclusion criteria  
                       *NICUs* (neonatologists and neonatal nurses)  
                       An NICU is eligible if it provides:  
                       a. intensive care for extremely preterm infants from birth  
                       b. incubator humidity in the care of extremely preterm infants  
                       c. written consent from Medical Director or appointed guardian  
                       *Patients (extremely preterm infants)*  
                       A newborn is eligible if:  
                       a. born less than 28 weeks gestation (inborn or out born)  
                       b. less than 24 hours of age  
                       *Exclusion criteria*  
                       *Patients*  
                       A newborn is not eligible if:  
                       a. there is a known congenital anomaly that could affect development  
                       b. death is imminent  
                       c. attendance for follow-up at 2 years is judged unlikely                                                                 |
| Study type          | Intervventional                                                                                                                            |
| Allocation: cluster randomisation, Intervention model: cluster assignment 1:4                                                                 |
| Masking: non-masked (parents, caregiver) masked (investigator, outcomes assessor)                                                                 |
| Primary purpose: reduce mortality and morbidity                                                                                                 |
| Target sample size  | To be confirmed                                                                                                                            |
| Recruitment status  | Not yet recruiting                                                                                                                          |
Primary outcome(s) | Death or survival with major disability at 2 years corrected for gestation
---|---
Key secondary outcomes | Proven late-onset sepsis, incidence of patent ductus arteriosus, chronic lung disease, intraventricular haemorrhage and necrotising enterocolitis

3. PROTOCOL VERSION

January-30-2013 | Original Version

4. FUNDING

The principal investigator and co-investigators will seek funding for the study from the relevant funding agencies.

5. ROLES AND RESPONSIBILITIES

A Trial Management Committee (TMC) will be established that includes the principal investigator, co-investigators and any additional members that may be invited to TMC meetings. The TMC will determine the roles and responsibilities of individual members.

INTRODUCTION

6. BACKGROUND AND RATIONALE

**Improving preterm infant health**

Extreme prematurity occurs in approximately 1% of live births [1]. Each year, in Australia, about 1,000 infants born less than 28 weeks gestation are admitted to neonatal intensive care units (NICUs) and approximately 75% are discharged home alive into the care of families [1, 2]. Unlike mortality, morbidity following extreme prematurity has not been reduced and despite nearly normal life expectancy, survivors are at risk of conditions such as chronic lung disease, sensori-neural disability, cerebral palsy, visual and hearing impairment, poor growth as well as cognitive, behavioural and educational deficits requiring frequent readmission to hospital, ongoing health care and additional educational and social services support [3–7]. Accumulating evidence has revealed how preterm birth affects adulthood with increased risk of psychopathology, in particular, attention deficit hyperactivity, anxiety, depression and behavioural problems [8, 9]. In addition, insulin resistance, higher blood pressure and decreased reproduction have been reported in adults born extremely preterm [10–13]. Reducing morbidities associated with extreme prematurity would enhance the quality of life for the infants and their families and reduce societal costs.

**Incubator humidity: Current practices and guidelines**

Incubator humidity has become a standard of care in the management of preterm infants in all NICUs in Australia and New Zealand [14]. Our team conducted a survey of humidification practices in NICUs across Australia and New Zealand [14] and a single-centre retrospective audit of patient medical records to assess effects of
introduction of incubator humidity on neonatal health outcomes. The work revealed a paucity of robust research evidence to guide decision making about humidification practices. The survey of incubator humidity practices found that this lack of robust evidence resulted in disparity between guidelines and wide practice variation both within and across NICUs because of differing clinician opinions about the benefits and risks of humidity use. The levels of humidity used in NICUs currently ranges from 60% to 100% and duration ranges from 3 to 77 days. Recently, Deguini et al. (2012) reported similar variability in incubator humidity practices across neonatal care units in France [15].

**Mechanism: Transepidermal water loss in extremely preterm infants**

Achievement and maintenance of thermal stability and fluid balance are major challenges in the management of the most immature infants. Existing evidence suggest that both thermal stability and fluid balance in the first days to weeks of life are important factors influencing neonatal morbidity [16–27]. Extremely preterm infants lose heat and water rapidly after birth primarily by evaporative means because of thin, functionally immature skin [28–35]. Fluid loss can be as high as 200 mL/kg/day [36, 37]. This high transepidermal water loss (TEWL) is inversely related to gestational age and decreases over time with increasing postnatal and gestational age [35, 38–47]. Reported complications of TEWL include hypothermia, weight loss, hyponatraemic dehydration, hyperglycaemia, hyperkalaemia, impaired renal function, metabolic acidosis, hyponatraemia, cerebral oedema, intraventricular haemorrhage (IVH) and death [36, 48–53]. Replacing huge losses may place the infant at risk for fluid overload, patent ductus arteriosus (PDA), chronic lung disease (CLD), necrotising enterocolitis (NEC) and death [16, 54]; therefore, methods to reduce rather than replace losses are essential. Neonatal clinicians use incubator humidity as a method to reduce evaporative losses.

**Existing Knowledge: Incubator humidity use in preterm infants**

Physiological studies suggest that the level of humidity is an important element in controlling evaporative heat and water loss in extremely preterm infants and have demonstrated reduced TEWL in infants nursed in highly humidified environments [19, 20, 41, 55–58]. An early randomised controlled trial of high versus low incubator humidity found that high-level humidity improved neonatal survival [20]. However, all infants in this study were hypothermic by today’s standards, and in subsequent RCTs conducted by the same research team, heat was provided to raise body temperature [19, 21]. No differences in survival were reported in the subsequent studies and the researchers concluded that the level of humidity provided no additional benefit. More recently, reported benefits from small, mostly retrospective studies of humidification include improved thermal stability, fluid balance and skin integrity [59–61]. However, optimal levels and duration of humidity for infants of varying gestational ages and the effects of humidification on clinically important neonatal health outcomes have not been determined. Specifically, there are concerns that a high level and/or prolonged use of humidity might increase sepsis risk.

**Incubator humidity: Levels and duration**

Optimal levels and duration of incubator humidity for preterm infants of varying gestational ages are unknown. Much of the physiological work that reported a reduction in TEWL used humidity levels around 80% in the first few days to weeks of life while TEWL is at its highest level [19–21, 41, 59]. Water loss to the skin ceases
when ambient humidity is 100% [56], but this can be difficult to achieve and maintain in the clinical environment. Further, the higher the level of humidity the greater the rainout or condensation within the incubator. This rainout, which results in damp bedding and moistens the infants’ skin, fuels concern about sepsis risk. It is not known whether lower humidity levels would provide benefits without increasing risk. One small RCT found that the provision of humidity greater than 70% beyond 14 days of life may increase TEWL and delay epidermal barrier maturation [57]. This finding supports animal and in vitro work that suggested transdermal water movement is the driving force behind barrier maturation and that skin matures more quickly in dry environments [62–65]. What this delay in skin maturation means for the extremely preterm infant is also unknown.

The literature offers little guidance on the optimal duration of incubator humidity. Although TEWL is highest immediately after birth and reduces over time, it still remains higher than that of a term infant at birth beyond four weeks of age in the most immature infants [32]. Kalia et al. suggested barrier function is attained at 30–32 weeks gestation [42]. Whether humidity is required during this time is a matter of debate; there is no consensus on when extremely preterm skin is functionally mature. Structural maturation occurs more rapidly following exposure to air. Researchers concerned about sepsis risk have recommended ceasing humidity as soon as clinically possible (1–2 weeks) [41].

**Incubator humidity and sepsis**

To date, the extent to which modern humidified incubators contribute to nosocomial infection rates remains untested. Studies of early humidifying systems reported the presence of microorganisms [45, 66–69]; however, recent modifications to humidifiers and the change in neonatal practices over time suggest that relating previous findings to modern-day practices may be inappropriate.

Reducing the risk of sepsis in this infant population is paramount. Sepsis is the major contributing factor to morbidity and mortality in extremely preterm infants [70–74]. Twenty to 58% of extremely preterm infants experience a serious systemic infection during their hospital stay [71, 75–80]. Mortality is as much as three times higher for infants who develop sepsis compared with those who do not [81] and accounts for approximately 50% of all deaths beyond the second week of life [82]. Complications associated with sepsis include CLD, PDA and NEC [75]. In addition, the literature describes poor growth and long-term neurodevelopmental sequelae including cerebral palsy (CP) and periventricular leukomalacia (PVL) in survivors [74, 83].

**Incubator humidity: Need for a trial**

There has been no improvement in morbidity following extremely preterm birth in developed countries. Therefore, neonatal clinicians are being challenged to evaluate not only the benefits and risks of new interventions but also those interventions that currently exist and are embedded in everyday practice. Incubator humidity use has increased and has been a standard of care for many years in some NICUs. Although there is a physiological argument to use humidity to reduce TEWL, there is no evidence of optimal levels and duration of humidity or its effects on important extremely preterm infant health outcomes. In particular, there is concern that a high level and/or prolonged duration of humidity may be contributing to sepsis rate. Whether incubator humidity contributes to current sepsis rates is uncertain because no
randomised studies have been conducted. However, it is a possibility because the warm, moist conditions created within the humidified incubator are intrinsically ideal for bacterial and fungal growth.

This study aims to answer longstanding clinical questions about incubator humidity use and to help to define optimal levels and duration of humidification. The study may help to reduce iatrogenic injury if a high level and/or prolonged use of humidity is found to have a negative influence on health outcomes. This would have the potential to benefit extremely preterm infants worldwide.

Choice of comparators
The following four comparators chosen in this study reflect the varying levels and durations of incubator humidity that are already current practice within NICUs across Australia and New Zealand:

1. Low level and short duration of humidity + normal care
2. Low level and long duration of humidity + normal care
3. High level and short duration of humidity + normal care
4. High level and long duration of humidity + normal care

7. Objectives

Research Hypothesis
Level and duration of humidity does not influence clinically important health outcomes in infants born less than 28 weeks gestation.

Primary Objective
To determine if level (low 60–70%, high 80–90%) or duration (short 14 days, long 28 days) of incubator humidity increases or decreases death or survival with major disability in infants born less than 28 weeks gestation at 2 years corrected for gestation.

Secondary Objectives

Key secondary objectives
The key secondary objectives are to determine, in extremely preterm infants, if level or duration of incubator humidity affects the incidence of:

- late-onset sepsis
- patent ductus arteriosus
- chronic lung disease
- intraventricular haemorrhage
- necrotising enterocolitis

Other secondary objectives
To assess the effect of level or duration of incubator humidity on:

- fluid balance
- growth
- length of initial hospital stay
- episodes of readmission to hospital up to 2 years corrected for gestation

8. Trial Design
The HIPI trial is designed as a cluster randomised, controlled, parent and caregiver unblinded multicentre equivalence trial with a primary endpoint of death or survival with major disability at 2 years corrected for gestation. Randomisation will be performed by cluster (NICU) with a 1:1 allocation.

METHODS

9. STUDY SETTING

To detect an intervention-related difference in death or survival with major disability at 2 years corrected gestation with the desired power; we chose to conduct the trial in NICUs in both Australia and New Zealand because a minimum of 16 NICUs (or clusters) are required to participate [84]. There are 19 NICUs in Australia and 7 NICUs in New Zealand.

All NICUs currently humidify the microenvironment in the management of extremely preterm infants [14]. The levels and durations of humidity used in the study reflect the variations in existing practice, and therefore, participation will not involve the introduction of a new intervention but may involve a new humidification practice for individual NICUs. Humidification practices will be standardised. Compliance with the trial protocol is dependent on consensus within NICUs to commit to the four proposed study arms.

10. ELIGIBILITY CRITERIA

Inclusion Criteria

NICUs (neonatologists and neonatal nurses)

An NICU is eligible if it provides:

a. intensive care for extremely preterm infants from birth

b. incubator humidity in the care of extremely preterm infants

c. written consent from Medical Director or person appointed as guardian of the cluster

Patients

A newborn is eligible if:

a. born less than 28 weeks gestation (inborn or out born)

b. less than 24 hours of age

Exclusion Criteria

Patients

A newborn is not eligible if:

a. there is a known congenital anomaly that could affect development

b. death is imminent

c. attendance for follow-up at 2 years is judged unlikely

11. INTERVENTIONS
A cluster randomisation design was chosen for practical reasons and to prevent contamination by preference of clinicians (selection bias) [84]. This multicentre randomised cluster study assesses the effects of two levels and two durations of incubator humidity on clinically important neonatal health outcomes. The clusters (NICUs) form the units of randomisation (or experimental units), and the individuals within the cluster (extremely preterm infants) form the units of observation. The intervention includes four variations in treatment (2x2 design): low level and short duration, low level and long duration, high level and short duration and high level and long duration where low level is defined as 60–70%, high level as 80–90%, short duration as 14 days and long duration as 28 days.

Eligible NICUs (clusters) will be randomly assigned to one of the four trial arms under investigation (see below).

1. Low level and short duration + normal care
2. Low level and long duration + normal care
3. High level and short duration + normal care
4. High level and long duration + normal care

Low level (60–70%), high level (80–90%), short duration (14 days), long duration (28 days) of humidity.

Implicit in clustering decisions is discussion with local clinicians regarding the definition of ‘normal care’. Any major differences in ‘normal care’ that has the potential to affect the outcomes of the study must either be standardised or stratified. An example of normal care that might affect the outcomes of the study is fluid administration protocols.

Calculation of sample size (the size and number of clusters) demands input from clinicians and statisticians who have the most up-to-date information on the numbers of extremely preterm infants within NICUs and knowledge of current outcome data. This will include calculation of the time needed to recruit sufficient numbers of infants and whether it will be necessary to recruit overseas to achieve the required sample size within an achievable time frame.

Randomisation of clusters to intervention arms will occur prior to patient admission. Infants less than 28 weeks gestation will be placed in incubator humidity within 6 hours of admission to the NICU according to the trial arm allocated. Humidity will be provided for a maximum of either 14 or 28 days depending on whether allocated to short or long duration. Hourly humidity levels and daily fluid requirements (mL/kg/day) will be documented on patient observation and infusion charts. Local research assistants will monitor compliance with protocol. All other care will be at the discretion of the members of the local multidisciplinary team. Because of the nature of the study, participating neonatologists, neonatal nurses, research assistants, other members of the multidisciplinary team and families within the NICUs will not be blinded to the intervention.

**Modifications**
For a given trial participant, the assigned study intervention may need to be modified or discontinued by trial investigators for various reasons including harm or health
status. To improve comparability across study groups and reduce subjectivity in care decisions, standard criteria for intervention modifications and discontinuations in the protocol will be defined. Regardless of any decision to modify or discontinue their assigned intervention, study participants should be retained in the trial whenever possible to enable follow-up data collection and prevent missing data.

**Adherence**

Success of the study is dependent on clinician commitment. A major priority of this study is the education and acceptance of the objectives of the study by all clinicians in participating NICUs. Other work by this research team identified wide practice variation and divergent clinician opinion relating to incubator humidity use [14], which could threaten trial fidelity by reducing its ability to detect differences in outcomes. This would require encouraging everyone involved in the study to have an inclusive and collaborative approach to maximise the likelihood that NICU clinicians would agree to participate. Face-to-face adherence reminder sessions will take place at the initial trial launch and each cluster visit thereafter. This session will include:

a. Aims of the study  
b. Provision of adequate knowledge about humidity and availability of equipment  
c. Procedures and data collection  
d. The importance of following the study guidelines and adherence to the protocol  
e. Consent at cluster level—posters and information forms for parents  
f. Encouragement to discuss any problems identified with local research assistant/investigator

Subsequent sessions will provide feedback on adherence and open discussion about progress and any issues identified. Information will be made available to all participating centres to maximise recruitment and ongoing efforts will be made to ensure high rates of follow-up such as newsletters and updates. All staff will have an opportunity to ask questions and key messages from the initial session will be reviewed as needed.

**Adherence Assessments**

To enhance validity of the data, the research team will assess adherence to intervention protocols. Research assistants will monitor levels and duration of humidity as recorded on patient observation charts. Adherence will be measured as the percentages of time spent in the target range (level) and the total number of days each infant received humidity (duration). This will be extrapolated to calculate the average difference achieved between study arms. This will be monitored by the Trial Management Committee (TMC), which will remain blinded to the outcomes for the four randomised groups. Only overall rates of clinical outcomes (for the four groups combined) will be provided to the TMC. In the event that an unacceptably small difference in humidity levels and duration is achieved, thus risking the possibility of underestimating any efficacy and harms, the TMC will consider strategies to preserve study power, including improving adherence at each site.

When non-adherence with the protocol or standard procedure occurs, one of the lead investigators for the study will contact the cluster site to resolve any issues. If appropriate, the issue will be referred to the TMC at their next meeting or by
correspondence with members if urgent. The HIPI TMC has full authority to take appropriate corrective action, including temporary or permanent withdrawal of the cluster from HIPI.

Concomitant Care
To attribute any differences in outcomes to effects of the study intervention and reduce co-intervention bias, discussion with clinicians in each cluster is essential to establish if the clusters have concomitant care practices or interventions (in addition to the trial interventions) that may affect trial outcomes. To promote comparability of clusters, the final version of the protocol will list the relevant concomitant care and interventions that are permitted, as well as any that are prohibited.

12. Outcomes

At this time, no core outcome set [85] exists for clinical trials of extremely preterm infants. The following outcome variables are valid, reproducible, relevant to the target population and responsive to changes in the health condition under study. These outcome variables (with the exception of fluid requirements) are used to assess the effect of varying interventions on extremely preterm infant health outcomes and could be used to form a core outcome set.

Primary Outcome Measure
Death or survival with major disability at 2 years corrected for gestation.

Major disability is defined as having any of the following:
- Cognition: Bayley, Mental Development Index MDI < 70 (-2SD)
- Neuromotor function: signs of cerebral palsy with inability to walk unassisted at 2 years corrected for gestation
- Severe visual loss: cannot fixate or is legally blind, corrected visual acuity < 6/60 in both eyes
- Hearing defect: diagnosis of deafness requiring hearing aid or cochlear implants

Secondary Outcome Measures
1. Proven late-onset sepsis (culture positive sepsis in blood or cerebro-spinal fluid occurring after 48 hours of age) in first 28 days
2. Patent ductus arteriosus diagnosed by ultrasound and requiring medical or surgical treatment
3. Chronic lung disease at 36 weeks postmenstrual age (oxygen dependency or respiratory support)
4. Intraventricular haemorrhage—all haemorrhage graded according to the criteria of Papile (grades I-IV) [86]
5. Necrotising enterocolitis requiring surgery

Other Outcome Measures
1. Daily fluid requirements (mL/kg/day) during first 28 days
2. Growth: weight, head circumference and length at birth, hospital discharge and at 2 years corrected for gestation
3. Length of initial hospital stay (days)
4. Readmission to hospital up to 2 years corrected for gestation (frequency, diagnosis)

13. Timeline

A clear and concise timeline (schematic diagram) will be developed and distributed to all clusters that includes the study process and procedures, interventions, assessments and time commitments for clinicians to guide trial conduct. These factors can also affect the decision of potential investigators and NICUs to join the trial.

14. Sample Size

With the assistance of a biostatistician, sample size will be calculated based on the primary outcome using a formal sample size calculation.

Sample size calculation will account for the study design. Because cluster randomisation is less statistically efficient than assigning individuals at random (unless there is no correlation within clusters), for the same statistical power, the overall sample size needs to be larger [84, 87]. Increasing the number of clusters increases the sample size.

15. Recruitment

Strategies to recruit NICUs to the study will be developed by the Trial Management Committee.

16. Allocation

Sequence Generation
Randomisation will occur at the cluster level (NICUs) rather than at the level of individual patients (CONSORT guidelines for cluster trials [84, 88]). Clusters will be randomly assigned to one of four groups as per a computer-generated randomisation schedule stratified by site, gestation (< 26 weeks, ≥ 26 weeks), gender, plurality and inborn or outborn.

Concealment Mechanism
Clusters will be randomised using the Clinical Trials Centre (CTC) central randomisation service. Allocation concealment will be ensured because the service will not release the randomisation code until clusters are identified and recruited and consent is obtained from the guardian of the participating cluster (NICU).

Implementation
All clusters who give consent for participation and who fulfil the NICU inclusion criteria will be randomised. Randomisation will be requested by the Medical Director or cluster guardian. All infants less than 28 weeks gestation who meet the patient inclusion criteria and are admitted into a cluster will be included in the study and will receive the allocated intervention.

17. Blinding
Because of the nature of the intervention, neonatologists, neonatal nurses, research assistants, other members of the multidisciplinary team and families will not be blinded to allocation. There will be blinding of the statistician responsible for the data analyses and the paediatricians and psychologists undertaking the outcome assessments.

18. DATA COLLECTION METHODS

Assessment of Primary Outcome
Paediatricians and psychologists who are unaware of the child’s incubator humidity interventions will assess all survivors at 2 years corrected for gestation.

Paediatrician will assess

- presence or absence of cerebral palsy, defined as loss of motor function in association with abnormal muscle tone or power
- weight, length and head circumference and calculate Z-scores
- data on hospital readmissions confirmed from the source

Psychologist will assess

- physiological assessment including the Mental Development Index and the Psychomotor Development Index on the Bayley Scales of Infant Development (Bayley III)

Ophthalmologist (if required) will assess

- vision

Audiologist (if required) will assess

- hearing

Assessment of Secondary Outcomes
The study will collect demographic data, several data points of interest at baseline and throughout the study period, and data on secondary outcomes from the infant’s medical records utilising electronic medical record systems when appropriate.

Assessment of Humidity
Levels and duration of humidity are recorded in patient observation charts; this will enable the monitoring of compliance with the study protocol.

The following will be recorded:
1. Level of humidity as recorded hourly (daily means will be calculated)
2. Duration of humidity (number of completed days)
3. Dates and times of commencement and cessation

Other data collected will include:

- gestational age
- birth weight
- Apgar scores
- plurality
- gender
- antenatal steroid use
- surfactant administration
- daily fluid requirements (mL/kg/day) for first 28 days of life
- time out of humidity per day (e.g. kangaroo care with parents)
- number of days received respiratory support
- number of days received oxygen therapy
- evidence and treatment of PDA
- evidence of IVH
- evidence of CLD at 36 weeks postmenstrual age
- evidence of NEC
- evidence of proven sepsis
- surgery

To ensure accuracy of data collection, a protocol of the process as well as data collection forms will be developed and study personnel will receive training. This training will be identical across clusters. The data to be collected will be reviewed in detail. Each of the data collection forms and the nature of the required information will be discussed on an item-by-item basis. Entering information into data forms, responding to data discrepancy queries and general information about obtaining research quality data will also be covered during the training session.

Retention

Clusters: Clinicians
Study investigators and trial co-ordinator will ensure:
- a collaborative approach
- regular communication with and feedback to all clusters
- ongoing interest in the study through materials and mailings
- use of newsletters and presentations to keep all clinicians up to date with the status of the study
- the support of everyone involved is acknowledged regularly

Clusters: Patients
Study withdrawal: Any infants who are prematurely discontinued from study humidity will be considered off study humidity/on study and will follow the same schedule of events as those infants who continue study treatment except for adherence assessment. All of these infants will be followed for up to 2 years corrected for gestation as scheduled.

The cluster study team will make every reasonable effort to follow the infant for the entire study period. It is projected that the rate of loss-to-follow-up on an annual basis will be at most 5%. This team are responsible for developing and implementing local standard operating procedures to achieve this level of follow up.

Parents
Cluster study teams will:
- provide written information and discuss study with all parents as soon as possible after admission
- provide regular feedback to all parents on progress of study
- send birthday cards and letters to parents prior to the 1 year and 2 year developmental assessment reminding them of the upcoming data collection
19. **DATA MANAGEMENT**

The TMC will approve data collection forms. Data will be managed and accuracy maintained by the Clinical Trials Centre (CTC) in collaboration with the local cluster study teams. Checks will be applied, weekly email reports with information on missing data, missing forms, and missing visits will be distributed by the CTC and, together with the local teams, it will be responsible for making any appropriate corrections. Written documentation of changes will be available via electronic logs and audit trails. Security, backup of data and the choice of hardware used will be the responsibility of the CTC [89].

20. **STATISTICAL METHODS**

Details of the approach to statistical analysis cannot be provided until clustering has been determined.

The primary analysis of this trial will be by intention-to-treat and will compare outcomes for mortality and major disability at 2 years corrected for gestation for all infants recruited. For secondary outcomes, adverse outcomes and protocol violations, analyses will be performed on all infants according to assigned treatment. Intention-to-treat analysis will take into account all participants, regardless of whether non-adherence to the protocol occurred at the individual or cluster level [90]. Intraclass correlation coefficients (ICC) will be determined and published for the primary outcomes variable.

Reasons for any withdrawals from each cluster will be recorded and compared qualitatively. The effect that any missing data might have on results will be assessed via sensitivity analysis of augmented datasets. Dropouts (essentially, parents who withdraw consent for continued follow-up) will be included in the analysis by modern imputation methods for missing data.

21. **DATA MONITORING**

A Data and Safety Monitoring Committee (DSMC) comprised of individuals of varying disciplines will be appointed by the TMC and will be independent of the study organisation. It will regularly review the outcome and safety data provided and report to the TMC.

An early meeting of the independent DSMC will be held with the TMC to discuss roles and responsibilities of the DSMC and agree terms of reference [89, 91–93]. Among the issues to be addressed are:

a. the need to assess net clinical benefit or harm as data accumulate
b. whether it is appropriate to specify futility as a criterion for recommending early closure [94]
c. the potential for an inappropriate recommendation of early closure that may arise from having multiple safety events (or harms) versus a single primary outcome (or benefit) of disability-free survival
d. the need for any surrogate outcome to fulfil stringent, pre-specified criteria, to be valid [95]
22. Harms

The standard definition of a serious adverse event (SAE) is any **untoward and unexpected** medical occurrence that:

* results in death or
* is life-threatening or
* requires inpatient hospitalisation or prolongation of existing hospitalisation or
* results in persistent or significant disability/incapacity or
* includes other important medical events (such as requiring surgery) that, in the opinion of the investigator, are likely to be serious if untreated, or as defined in the protocol

Since most of these events are common in extremely preterm infants, the proportion of **unexpected serious adverse events** (in the opinions of the investigator) is expected to be small. Unexpected SAEs are to be recorded and reported. They will be notified to the coordinating centre within one working day of the event becoming known to the local investigator. This will activate a notification cascade, which includes notifying the lead human research ethics committee (HREC), the Data and Safety Monitoring Committee, the Trial Management Committee and all principal investigators participating in the study.

The Therapeutic Goods and Administration (TGA) will also be notified of SAEs in accordance with TGA regulations. The investigator or delegate at each participating hospital is responsible for reporting SAEs to their local HREC. This may require a change to the Parent Information Sheet: the coordinating centre would be informed of any changes. The Data and Safety Monitoring Committee will monitor unexpected SAEs at least on an annual basis.

23. Auditing (Quality Assurance)

Data Handling and Record Keeping

Trial data will be recorded on electronic case record forms that will be developed for this purpose. All required data entry fields will be completed. Data corrections will be made according to the instructions provided. The investigator will confirm the accuracy of completed forms by signing them as indicated.

Source documents pertaining to the trial will be maintained by investigational sites. Source documents may include a subject’s medical records, hospital charts, clinic charts, the investigator’s subject study files, as well as the results of diagnostic tests such as X-rays, laboratory tests, ultrasounds and electrocardiograms. The investigator’s copy of the case report form serves as part of the investigator’s record of an infant’s study-related data.

The following information should be available from the infant’s medical record so that it can be entered later into the electronic data form:

a. Infant’s name, parents’ details, contact information and study number
b. The date of NICU consent
c. The date and time that humidity was commenced
d. Any unexpected serious adverse events
e. The date humidity was ceased

All study-related documentation is subject to independent review and will be maintained for 15 years following completion of the study [96].

**Study Monitoring**
Data from this study will be monitored by the Clinical Trials Centre (CTC), Sydney. An audit manual will be developed. Monitoring will include centralised review of data forms and other study documents for protocol compliance, data accuracy and completeness. Monitoring may include monitoring visits to investigational sites for source data verification and review of the investigators' site files. The CTC will have direct access to source documents and study-related documents.

**Audit and Inspection**
This study may be subject to audit or inspection by representatives of the CTC or representatives of regulatory bodies such as the Therapeutic Goods Administration.

**Clinical Study Report**
The CTC will enter and analyse the data. A Clinical Study Report will be issued that may form the basis of a manuscript intended for publication. The TMC will approve the Clinical Study Report or summary thereof.

**Accountability of the Study Treatment**
The study intervention is incubator humidity. Each participating NICU has incubators that provide humidity, and incubator humidity is currently an existing standard of care in all centres. This study is not introducing a new intervention but rather is assessing the benefits and risks of the variations in humidification practices that currently exist within NICUs.

**ETHICS AND DISSEMINATION**

**24. Research Ethics**

Lead and site-specific institutional ethics approvals will be sought. Additional information will be provided regarding the cluster design and implications of this for the consent process.

**25. Protocol Amendments**

Any modifications to the protocol that may affect the conduct of the study, potential benefit of the patient or patient safety, including changes of study objectives, study design, patient population, sample sizes, study procedures or significant administrative aspects, will require a formal amendment to the protocol. The TMC will agree on such amendment, obtain Ethics Committees approval prior to implementation, and notify the appropriate organisations in accordance with local regulations. Administrative changes of the protocol are minor corrections and/or clarifications that have no effect on the way the study is to be conducted. The TMC
will agree on these administrative changes, which will be documented in a memo.

The Ethics Committees may be notified of administrative changes at the discretion of the TMC.

26. CONSENT OR ASSENT

Informed consent will be obtained at a cluster (NICU) rather than at individual patient level. The principal and co-investigators will obtain consent from the Medical Directors or cluster-appointed guardians prior to randomisation and allocation. Information about the study will be provided to parents.

27. CONFIDENTIALITY

The study will be conducted in accordance with applicable privacy acts and regulations [96]. All data generated by this study will remain confidential. All study-related information will be stored securely at the cluster sites. All participant information will be stored in locked file cabinets to which only those involved in the study will have access. All laboratory specimens, reports, data collection, process and administrative forms will be identified by a coded ID (identification) number to maintain participant confidentiality. All records that contain names or other personal identifiers will be stored separately from study records identified by a code number. All local databases will be secured with password-protected access systems. Forms, lists, logbooks, appointment books and any other listings that link participant ID numbers to other identifying information will be stored in a separate, locked file in limited-access areas.

28. DECLARATION OF INTERESTS

Any competing interests or conflicts of interest that exist between individual investigators’ private interests and their responsibilities to scientific and publishing activities will be declared.

29. ACCESS TO DATA

The Trial Management Committee will decide who has data access.

30. ANIMAL AND POST-TRIAL CARE

The Trial Management Committee will decide if ancillary or post-trial care is required.

31. DISSEMINATION POLICY

The TMC will appoint a Writing Committee to draft manuscripts based on the study data. Manuscripts will be submitted to peer-reviewed journals. The first publication will be the report of the full trial results based on the main protocol using the study group name, with subsequent publications of data subsets. The Writing Committee
will develop a publication plan including authorship, target journals and expected
dates of publication. Plans, if any, for granting public access to the full protocol,
participant-level dataset and statistical code will be decided by the TMC.

32. APPENDICES

There are no appendices at this time.

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So far, this chapter has presented the protocol for a CRCT. I will now provide a critical analysis of the design and feasibility of the trial given the variability in humidification practices, the complexity of the contexts and the individuals within them, and the reality of conducting a large trial in the face of real threats to fidelity. Finally, I will discuss the change in the focus of the work, which prepares the reader for Chapters 7 and 8.

6.3 Critical Analysis of Study Design and Feasibility

The study design itself posed several challenges. The following section provides rationale for choosing a cluster randomised design and describes the implications of that choice. Further, this section discusses implications of the decision that to answer the research questions required a multicentre study and the feasibility of achieving this within the thesis timeframe given my knowledge of the complexity of the NICU contexts.

6.3.1 Challenges of study design

A pragmatic CRCT was the chosen methodology—pragmatic in that we designed the study to help choose between four care options applied in routine practice (Eldridge & Kerry 2012) and a cluster trial in which groups or clusters of individuals (NICUs) rather than individuals themselves are randomised to the intervention arms (Eldridge & Kerry 2012). The clusters (NICUs) form the units of randomisation (or experimental units), and the individuals within the cluster (extremely preterm infants) form the units of observation. Outcomes in this trial would be observed at the individual level. The distinction of the two ‘units’ recognises the differences between the CRCT and the traditional type of RCT (Eldridge et al. 2008; Eldridge et al. 2004; Eldridge & Kerry 2012; Guittet, Ravaud & Giraudet 2006; McRae et al. 2013; Taljaard et al. 2009; Weijer et al. 2011).

The literature provides evidence of increasing use of CRCT methodology in neonatal trials (Acolet et al. 2011; Kirkwood et al. 2010; Lee et al. 2009; Wallin et al. 2011). Although it is more complex, we chose a cluster randomisation design for practical reasons to prevent contamination by preference of clinicians within each NICU
We based our decision to use cluster randomisation on our knowledge of the wide practice variation and divergent clinician opinion about incubator humidity that might affect the success or failure of the trial, thus attempting to reduce potential threats to trial fidelity. Put simply, this means that each cluster or NICU would be randomised to only one of the four trial arms. However, participation in the study would require local consensus on the study interventions and, given the complexity of the NICU contexts and that humidity use is a contentious issue, this might prove challenging if not almost impossible.

Choosing CRCT methodology had implications for the design, conduct and analysis of the study. Eldridge and Kerry (2012) provide an excellent guide to aid clinicians’ understanding of CRCTs. A discussion of the full content of the guide is beyond the scope of this chapter, but I will highlight three key challenges reported by the authors: sample size calculation, data analysis and ethical dilemmas. The first two challenges relate to sample size calculations and data analysis. Compared with an individually randomised trial with the same number of individuals, cluster trials are inefficient and have less statistical power (Campbell, Donner & Klar 2007). This added complexity arises primarily because observations on individuals within the same cluster may be correlated—that is, the outcomes for individuals within clusters are likely to be more similar than those across clusters (Campbell et al. 2012).

For the same statistical power, the overall sample size needs to be larger in a cluster randomised trial than in an individually randomised trial. The reduction in effective sample size is dependent on average cluster size and the degree of correlation within clusters (Campbell et al. 2012). The statistical measure of this ‘clustering effect’ is known as the intracluster correlation coefficient, or ICC (Donner & Koval 1982). Analysis involves calculation of an ICC for each outcome variable. The ICC for a particular outcome defines the amount of variation in the dataset that can be explained by the variation between clusters. Adjusting for intracluster correlation reduces statistical power. Therefore, sample size is achieved best by increasing the number of clusters rather than the cluster size (Campbell et al. 2012; Campbell et al. 2004; Feng et al. 2001; Guittet, Giraudeau & Ravaud 2005; Kerry & Bland 1998), and thus recruitment of large numbers of NICUs is essential to the success of the proposed trial.
Eldridge and Kerry (2012) recommend a minimum of four clusters for each trial arm, which means that the trial would require the participation of at least 16 NICUs.

The third challenge of CRCTs relates to ethics, which is particularly complex. There is a growing body of published literature on the ethical issues raised by cluster randomised trials that pose serious challenges to the current conceptual research ethics framework. Consequently, HRECs and regulators have no single international standard to guide their review of cluster trials (McRae et al. 2013; Taljaard et al. 2009; Weijer et al. 2011). This lack of standardisation has resulted in uncertainty and markedly different interpretations of permissible practices within cluster trials (Weijer et al. 2011). Weijer and colleagues (2011) provide an informative overview of the many ethical implications of CRCTs. A discussion of all of these is beyond the scope of this chapter, but one in particular is worth mentioning here: the subject of informed consent. This is a controversial issue because researchers obtain consent at the level of the cluster (NICU) rather than at the level of the individual patient. Recommendations include the provision of detailed information about the study for all patients and their families (Eldridge & Kerry 2012). In addition, site-specific ethics committee approval is required for each site participating in the study, but varying HRECs may have varying views on cluster studies. I know from my own experience as member of a lead HREC in Sydney that this particular committee does not support studies that do not request individual patient (parent) consent. It is interesting to consider that there are additional HREC hurdles to jump over in the design and conduct of CRCTs. This is somewhat ironic given that incubator humidity is a routine practice and day-by-day, shift-by-shift variability is commonplace in NICUs.

One further issue to highlight in discussing ethical dilemmas is the issue of not recruiting those patients whose follow-up researchers’ judge unlikely; the reader may have noticed this inclusion in the study protocol. This finding is commonplace in the protocols of multicentre neonatal trials in Australia (Stenson, Brocklehurst & Tarnow-Mordi 2011; The INIS Collaborative Group 2011), hence its inclusion in our protocol. However, I do challenge this inclusion. Excluding patients based on geographical location and difficulties of access for the purpose of follow-up reduces various socio-demographic characteristics and introduces significant bias by removing from the study a high risk and most disadvantaged group who live in remote areas across Australia.
Therefore, study results cannot be generalised to all Australians. Future studies need to address these inequalities and ensure the provision of adequate resources to enable implementation plans to include the collection of outcomes from those not currently included in clinical trials.

6.3.2 Challenges to trial feasibility

The many layers of complexity identified throughout the work of the thesis made me realise that the plan to conduct the proposed study was no longer viable and beyond the scope of my doctoral work. The decision that the study should be powered sufficiently to assess the benefits and risks of incubator humidity on long-term health outcomes meant the need for a large multicentre trial. Such a study would be logistically challenging and require a grand design and a huge investment in time, money and people. The enormity and complexity of the task soon became apparent. My increasing understandings of the multiple issues that we would need to overcome to make such a trial feasible were prohibitive and the number of potential confounding variables was overwhelming, even if time and resources were available. Further, the trial (as in all large multicentre trials) would take years to complete, even if the planned sample size was achieved within the timescale, which is a reality for many studies (McDonald et al. 2006), and it would take even longer before results could be available, much less influence patient care. This process could be further complicated by the fact that recruitment of neonatal (and paediatric) patients to clinical trials in Australia takes on average 18 months longer than in adult trials (Tarnow-Mordi, Simes & Cruz 2013).

To design and execute such a clinical trial would require that we pay due attention to the complexity of the practice environment. Farrell, Kenyon and Shakur (2010) suggested that science alone is not sufficient to successfully deliver a trial. Other authors have identified site selection (Hague, Gebski & Keech 2003), interdisciplinary collaboration (Fry, Mortimer & Ramsay 1994), strong leadership and good communication (Kutner et al. 2010) as being vital to successful trials, whereas variation in practice and individual clinician preference have proven to be obstacles (Anyanwu & Treasure 2004). This evidence supports the notion that the implementation of trial protocols could have unintended consequences unless there is meaningful engagement of clinicians,
encouragement of their involvement in the production of evidence and local consensus on trial objectives.

6.4 Reflections, Learning and Critical Questions

I reflected on the work of the thesis to date and on other RCTs in which I had been involved in some way. Naively, it had never occurred to me that there had been violation of trial protocols, which had unknown implications for the results and the subsequent recommendations. Therefore, I questioned how RCT methodology, recognised as having the scientific credibility and rigour necessary to inform clinical decision making (Hicks 1998), could account for the multiple confounders within complex practice environments. The inference is that experimental evaluation is flawless, a means of ensuring certainty. This reflection led me back to the literature—this time with very different eyes. In the following section, I move my attention from the post-positivist world of the RCT and use an alternative lens through which to view the research process.

6.4.1 An alternative viewpoint

The basic tenet of the RCT is the theory of causation. Using our proposed RCT as an example, the process begins with four groups of extremely preterm infants, the assumption being that these groups of infants are identical. The only differences between the groups are the incubator humidity interventions allocated; therefore, the next assumption is that one of the interventions caused the outcomes observed. As we cannot observe causation, causation between interventions is inferred from the repeated success of one of the interventions over the others. This assumes the exclusion of all confounding variables with only one remaining causal link (Pawson & Tilley 1997). This methodology does not account for individual patient differences or experience and information from the local context.

In the discipline of philosophy, the epistemological literature (the study of knowledge and knowing) refers to this way of thinking as a successionist or molar understanding of causality (Hume 2003). An alternate viewpoint, that of ontology (the study of the
existence, nature or being of a certain entity), considers the complexities and messiness of the social world and suggests that many mechanisms operate simultaneously in the presence of certain contextual conditions (Pawson & Tilley 1997). This poses challenges for the epistemological view of world of the RCTs that assumes the intervention (or one of the interventions) caused the outcome. Therefore, ontology considers the assumptions of epistemology over simplistic. Critics claim RCT methodology is popular for this very reason because it rationalises complex social processes by eliminating culture, contexts and the subjects of knowledge production from consideration (Goldenberg 2006), thereby simplifying the research process.

Realist evaluation, which is based on philosophical realism, has been proposed as an alternative to experimental evaluation (Pawson et al. 2005; Pawson & Tilley 1997). Realism sits between the extremes of positivism and relativism (McEvoy & Richards 2003; Pawson & Tilley 1997) and acknowledges the world as an open system with structures and layers that interact to form mechanisms and contexts. Pawson and Tilley (1997) developed the basic realist formula of mechanism (M) + context (C) = outcome (O), by which realist evaluation aims to identify causal mechanisms, how they work and under what conditions (McEvoy & Richards 2003; Pawson et al. 2005; Wilson & McCormack 2006). Since causal mechanisms are inherent in specific contexts and social processes, there is a need to understand the complex relationship between these mechanisms and the effect that context has on their operationalisation and outcome (Rycroft-Malone et al. 2010). Therefore, realist evaluation asks the questions: what mechanisms work? for whom? in what circumstances? why? to produce which outcomes? (Pawson & Tilley 1997; Rycroft-Malone et al. 2010)

Thus, from a realist perspective, the aim is not standardisation and generalisability, as is the case with the RCT and meta-analysis, but rather it is about working with evidence and synthesising it while taking account of the local context, local clinicians and the patient population. What this viewpoint suggests is that working with the variability in local contexts and acknowledging the confounders is vital to successful implementation of research and, therefore, may be fundamental to study design. Study design needs to embrace confounders, not attempt to strip them away. This brings into question the methods of the multicentre RCT and the generalisability of results. Although large trials
might make data statistically meaningful, this way of viewing the world questions whether results can be clinically meaningful or generalisable to differing clinical contexts given that the trial is conducted in what trialists refer to as a ‘context-free’ environment? What ‘works’ within the trial environment may not do so in the real and complex world of the practice. Similarly, it could be argued that no environment is ever context free, whether during the conduct of a trial or not; many confounders might be influencing the results.

This literature and my learning during the years of the thesis challenged my deeply held beliefs, my assumptions, my desire for certainty and my whole way of thinking about research. Had we proceeded with the RCT without taking a systematic approach to the work—without uncovering the complexity both of humidification practices and the ‘messiness’ of the various practice environments—is it possible that the study would have failed to achieve its goals? If it is true that acknowledging context and external influences is the key to success, and if RCTs and grand designs are required to answer some clinical questions, what must these designs look like to ensure we consider all these factors? What would our proposed research look like from a realist perspective? Our research questions could ask how clinicians operationalise the intervention of incubator humidity within varying clinical contexts and how it affects clinical practice, the individuals and the patients. The design of such a study would be immensely complex and would require the unpacking of the relationships between context, mechanisms and outcomes that would probably need some additional thinking through to ensure the multiple factors involved received adequate consideration. How would neonatal clinicians accept such a study? I think it is unlikely they would accept this methodology at this time. Clinicians, administrators and policymakers rely exclusively on the certainty of EBM with its gold standards to inform decisions about neonatal care. Philosophical arguments are a little more tenuous; perhaps we should heed Blair’s (2004, p. 1219) warning that ‘gold is not always good enough’.

6.4.2 What do the findings of this chapter mean for the proposed study?

Following discussion with my supervisors, and with the aim of completing the thesis, it was agreed I should conduct a pilot study within my workplace and report the results in
the final chapter. Sadly, deteriorating interpersonal relationships and conscious or unconscious threats to feasibility thwarted attempts to conduct the pilot study; incubator humidity continued to be a controversial and emotive subject. Once again, this confirmed the influence of individuals on what is possible within the practice environment. The inability to conduct the pilot study in my workplace was the ‘final straw’ for the thesis plan. My search for certainty had proved to be far more elusive than I had first thought.

Events within my workplace confirmed the key finding of the work of the thesis: the overarching influence of complex NICU contexts and the powerful effect individuals have on relationships in the practice environment, the generation of new knowledge and clinical practice. I now had very different questions to ask. How do we generate new knowledge and implement research findings given the diversity in practice environments and the belief systems of the individuals who provide care? What ways of collaborating are most likely to be effective in the future? Since we no longer planned to conduct the trial and it appeared no other research teams were doing similar work, what should neonatal clinicians do in the interim about the use of incubator humidity? If we want to reduce inconsistency and uncertainty for clinicians and parents, we need an evidence base for practice, whether that is in the generation of new knowledge or in some form of local consensus on practice based on a synthesis of the knowledge that already exists. Since change and uncertainty are now part of everyday life in a complex health care world, we need to find ways to work creatively so that we can embrace change, deal with uncertainty, and improve patient care in an environment where individuals can grow and flourish. Perhaps first we need to understand what constitutes an effective workplace culture and what drives human behaviour and how individuals relate to each other. These questions changed the focus of the final chapters of the thesis.

6.5 Chapter Summary

In this chapter, I presented an example of what a protocol for a CRCT investigating the effect of varying levels and duration of incubator humidity on neonatal health outcomes might look like. Information gained from the work of previous chapters informed the
trial design and development of the protocol. I also presented a critical analysis of the study design and the feasibility of conducting a large-scale multicentre study within the time frame of the thesis. I reflected on the implications of the findings to date and this was the turning point of the thesis; even if time (and funding) were available, the work identified much broader issues that we would need to address for the proposed trial to be successful. Clinical contexts and, in particular, the individuals within those environments who drive decision making influence what happens in everyday practice irrespective of available research evidence. Acknowledging this influence and the effect of interpersonal relationships on local culture, clinician wellbeing and patient care, I had another question to ask, where to from here?

In giving up the idea of undertaking an RCT as the ‘best way’ to improve care to patients and families I realised that the complexity that surrounds care of extremely preterm infants in NICUs means that a broader and more multifaceted way of thinking about practice innovation and best practice is needed. Therefore, I sought broader models that allowed me to think about the workplace cultures in which these infants are cared for and the nature of the individuals providing the care. The next chapter reflects on my research journey and the NICU environment and seeks to understand more about context and determine what constitutes an effective workplace.
Chapter 7: C’ing a Way Forward: Seeking to Build More Effective Workplace Cultures

7.1 Chapter Overview

In this penultimate chapter, I draw together and critically analyse the findings of the thesis. The major finding highlighted is the importance of the practice environment or context on knowledge generation and utilisation, and patient care. Failure to optimise the physical environment, deal effectively with complex and dynamic workplaces, work creatively with the resources and research evidence available, and develop healthy relationships to create an effective workplace culture negatively affects the wellbeing of clinicians, parents and infants. We need to create workplace cultures that acknowledge and embrace existing complexity and inevitable change, and promote healthy relationships that enable clinicians and families to work collaboratively in the generation and utilisation of research evidence to ensure positive patient outcomes. An important first step in achieving these aims might be to raise awareness of the contextual realities that exist within the NICU environment, the relationships among the myriad of characters that make up the multidisciplinary team responsible for the care of infants and families, and the difficulties that arise when multiple characters seek certainty in the face of overwhelming complexity.

In the first section of this chapter, I reflect on my research journey, the decisions made and how these shaped the work of the thesis. Recognising the influence of workplace culture on this work the second section seeks to understand more about context, how it contributes to the workplace culture and how to determine what an effective workplace culture might look like. In the third section, I provide a critical exploration of the NICU context, in general, and within my workplace, in particular. The chapter concludes by proposing a way forward that has the potential to improve the way clinicians relate to each other and create effective workplace cultures.
7.2 My Research Journey

I began this journey seeking evidence of the most effective level and duration of humidity for extremely preterm infants nursed in incubators. This goal was in response to my observations of care that revealed much controversy and inconsistency in humidification practices and recognition of the need for practice change in my workplace. The work proved timely and complemented urgent calls from health care to assess the effectiveness not only of new but also of existing interventions to ensure positive patient outcomes. My end goal was to resolve an issue that plagued clinicians working within NICUs everywhere. It was an ambitious goal, but one driven by my passion to play a role in generating clear guidelines to reduce the inconsistencies and uncertainty faced every day in every NICU across the globe. Instead of the certainty I sought my research painted a picture of overwhelming complexity—complexity in terms of the nature of the work and the NICU environment, in terms of the characters leading and practising within those units and, in particular, in terms of incubator humidity practices and in the generation of research evidence that would enhance the sense of certainty about humidification.

As the work progressed, I became increasingly aware of the many layers and depth of this complexity. The evolution of, and evidence for, incubator humidity presented in Chapter 2 revealed several factors that influenced the care of preterm infants—factors that I have come to discover persist today. These factors included political agendas (e.g. eugenics), the influence of context (France versus the United States), the challenges of and time taken to implement change (the introduction of the incubator) and the beliefs, attitudes and influence of individuals or characters in the change process (Tarnier [Budin 1907] and Couney [Silverman 1979]). Further, the history books describe sporadic use of humidified incubators based on the beliefs of various individuals of the time, much as it is today. Both this broad review of the literature and the systematic review of RCTs reported in Chapter 3 found little robust evidence of optimal levels and duration of humidification or of the effects of humidity use on long-term health outcomes. These findings validated the need to address the initial research questions I had posed. However, the process of systematic review also proved more complex than I had anticipated. During the review process, I again encountered the powerful influence
of individual characters—this time in the generation and publication of knowledge. Failure to achieve meaningful engagement and consensus on the interpretation of existing literature on incubator humidity with the CNRG has meant that, to date, the systematic review remains unpublished.

As the work evolved, the role of context and, in particular, the characters within the workplace took centre stage. In undertaking the survey of humidification practices in NICUs across Australia and New Zealand reported in Chapter 4, I discovered other clinicians grappling with issues related to humidification similar to those I had experienced in my workplace. I found incubator humidity practices to be inconsistent both across and within NICUs; humidification was indeed a controversial and highly emotive subject. Such variability was echoed in a recent review of incubator humidity use in France (Deguines et al. 2012), thus confirming that this continues to be an important clinical issue in NICUs.

In the absence of clear evidence or consensus, local contextual factors influence practice; I had not anticipated such wide variation in practices. The inconsistencies in practices, I was to discover, were not solely caused by the lack of research; profound differences in the interpretation of available evidence, established routines and varying clinician beliefs and opinions also shaped practice decisions. Where CPGs did exist, the extent to which clinicians used them varied. According to the participants of the survey, disruptive behaviour, difficult interpersonal relationships, a lack of effective leadership and the influence of those in management roles appeared to compound the problem in some NICUs; these findings reflect my own experiences within the workplace. Collectively, these issues created uncertainty and frustration for clinicians and parents at the bedside. I found similar inconsistencies in practice and further evidence of the potent influence of individual characters when conducting the audit reported in Chapter 6. The audit sought to determine whether patterns existed between the introduction of incubator humidity and short-term neonatal health outcomes. The non-comparability of the groups meant that this audit failed to identify any such patterns; however, it did provide me with a wealth of information about the context of the practice environment, how clinicians used guidelines and the influence of individual characters on others and on patient care.
After analysis of the audit data, I came to realise that I would be unable to conduct an appropriate RCT, or even a comprehensive pilot for such an RCT. There were three major reasons for this. The first was the conclusion arrived at by our multidisciplinary research team that, to answer my research questions, a large multicentre trial would be required; I knew I could not conduct a study of this magnitude within the thesis timeframe. A large multicentre neonatal trial is a complex undertaking and incurs sizable costs in time, money and people, including a diversity of support roles. International collaboration is usually necessary to accrue the required samples of hundreds or thousands of extremely preterm infants. The conception, planning and design of the study may take several years, with several additional years in implementation, subject follow-up, data analysis and publication. Further, I came to realise that, along with the knowledge generated through an RCT, paralleling work would need to be undertaken to prepare NICUs to embrace and implement evidence produced through such a trial.

The second reason for relinquishing the goal of conducting the trial and of greatest concern to its planning and design was the dissonance I found between the rhetoric and the reality of RCT methodology. My increasing awareness and understanding of potential flaws in empirical research (Oakley 2000; Pawson et al. 2005; Pawson & Tilley 1997) led me question whether, in fact, RCT methodology would answer the research questions. RCT methodology rationalises complex social processes by not acknowledging confounders within the practice environment, such as culture and context (Goldenberg 2006). What ‘works’ and is clinically meaningful in this ‘context-free’ trial environment might not be so effective or be appropriate in varying clinical contexts. Further, evidence suggests the workplace culture can bias research (De Vries & Lemmens 2006). How then can we ensure that the biases, beliefs and preferences of researchers and clinicians in various clinical settings will not influence the conduct of a clinical trial? In this work, the inconsistencies in practice, the variability in guideline use and the varying opinions and beliefs about the benefits and risks of humidification across and within NICUs threatened the fidelity of a trial that required local consensus and protocol adherence.
The third reason for not conducting the trial magnified these doubts about the robustness of RCT methodology. The variability and complexity within clinical contexts and my increasing understanding awareness of the context-specific nature of knowledge generation and utilisation as identified and described by Scott and colleagues (Scott-Findlay & Golden-Biddle 2005; Scott et al. 2008; Scott & Pollock 2008) meant that I was unsure which questions I would be able to answer. As researchers, we need to consider the uniqueness of each practice environment and the individuals who provide the care if successful knowledge generation and utilisation are to become a reality. Further, individual characters within my workplace who opposed the use of humidity thwarted plans to conduct a pilot study. The reality that I would be unable to conduct this study was very disappointing for me initially. This reality and my newly found desire to make sense of my findings and experiences led me to choose a very different path.

On summing up my experiences and learning, one finding had struck me the most during my research journey: the role context played in the use of incubator humidity, the standardisation of practice, the generation of new knowledge generation and the utilisation of existing research evidence. Further, within those clinical contexts, the influence of ‘human factors’—for example, the effect of interpersonal relationships, individual or group, and social processes on everyday practice and workplace culture—was enormous. Consequently, I sought to gain a deeper understanding of how context influences clinical practice and identify what factors constitute an effective workplace. In addition, I wanted to gain insight into what drives human behaviour and understand how we might use these insights to improve professional relationships and the way teams work. To achieve these aims, I returned to the literature, this time with very different eyes and asking very different questions. I consulted the literature of other disciplines, including implementation science, management, business, philosophy, social psychology, social neuroscience and neuroleadership. Exploring the literature led me to a very different approach; this chapter addresses the topic of effective workplace cultures and the following chapter seeks to identify the drivers of human behaviour within those cultures.
Realising the complexity that surrounds care of extremely preterm infants in NICUs, I sought a broader and more multifaceted way of thinking about practice innovation and best practice. Therefore, I sought broader models that allowed me to think about the workplace cultures in which these infants are cared for and the nature of the individuals providing the care; I found the implementation science and practice development literature. The challenges of transferring research evidence into behaviour change and improved patient outcomes gave rise to the development and/or refinement of numerous models, theories and frameworks, all with the same goal: to overcome the barriers to knowledge translation (Conklin & Stolee 2008; Greenhalgh et al. 2005; Kitson, Harvey & McCormack 1998; Kitson et al. 2008; Rogers 1983, 1995; Rycroft-Malone et al. 2002). These models, theories and frameworks were instrumental in raising awareness of the importance of context in the success (or failure) of research implementation and of innovation in general. The following section seeks to increase understanding about the important elements of the clinical context and then determine the attributes of an effective workplace culture.

7.3 Understanding Workplace Context

No one overarching implementation theory exists and many different terminologies and definitions are used in writings on the topics relating to the transfer of knowledge, including quality assurance, quality improvement, research utilisation, knowledge utilisation, knowledge translation, knowledge transfer, knowledge-to-action, dissemination science, innovation diffusion and implementation science (Estabrooks et al. 2006; Grimshaw et al. 2012; McKibbon et al. 2010; Tetroe et al. 2008). In fact, McKibbon et al. (2013) recently identified more than 100 terms that are used by those interested in translating evidence into practice. Many of the theories and models developed to improve practice (change behaviour) have targeted individual clinicians (Rogers 1983, 1995), local practice environments (Kitson, Harvey & McCormack 1998; Kitson et al. 2008; Rycroft-Malone et al. 2004) and whole organisations (Greenhalgh et al. 2009; Greenhalgh et al. 2005; Schein 1992). I discovered significant overlap in the included elements when comparing the theories and models, although each omitted some of the elements included in others. However, what this existing work has identified is that one element—context—is crucial to a healthy work environment and
successful practice change. Although I reviewed a substantial number of the published
theories and models, initially I chose two of the most commonly used to gain insight
into context, the Diffusion of Innovations (DOI) conceptual map and the Promoting
Action on Research Implementation in Health Services (PARiHS) framework.

An innovation is an idea, a technology, a research discovery, a way of working—
anything that is perceived as new and that requires a change of hearts and minds and
structures and systems to become business as usual (Greenhalgh et al. 2004). Although
innovation is a broader concept than the implementation of a CPG or other practice
change, the DOI conceptual map (Figure 6) is very relevant to the processes involved in
research uptake and utilisation in health care. Implementing an innovation means
change, and a vast body of literature exists that describes change management; however,
a discussion of this is beyond the scope of this chapter.

Figure 6: Diffusion of Innovations Conceptual Map (Greenhalgh et al. 2004)

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As a theory, DOI has a long history of both conceptual and empirical study. The earliest reference to DOI research is attributed to the French lawyer and social psychologist Gabriel Tarde, whose interests lay in understanding why some innovations spread widely while others do not (Tarde 1903; Toews 2003). Ryan and Gross (1943) later introduced the adopter categories; Katz (1957) added the concept of opinion leaders and opinion followers, and Rogers, in four editions of his book *Diffusion of Innovations*, was responsible for its popularity and, through the synthesis of the work of other researchers, refinement of the theory (Rogers 1962, 1983, 1995; Rogers & Shoemaker 1972). Classical DOI as illustrated by Rogers developed around a body of work that identified a consistent pattern of adoption of new ideas over time by people in a social system. Early versions focused on the characteristics of the individuals involved in the innovation, and ongoing refinement of DOI recognised the influence of other factors including context.

More recently, Greenhalgh and colleagues (Greenhalgh et al. 2005; Greenhalgh et al. 2004) synthesised the DOI research; this culminated in the development of a conceptual map and recommendations for its application within health care organisations and for future research. The conceptual map presented by the authors is detailed and very complex with an emphasis on organisational rather than local workplace change—the focus of this work. The map highlights the clinical context, individual characters, transformational leadership, skilled facilitation and resources as important factors in the success or failure of implementation of an innovation. What is less clear is how to identify and work with the complexity within each element or factor and the possible interactions or relationships between them. Further, the authors acknowledge that literature from cognitive psychology, which identifies individual characteristics or personality traits associated with an individual’s propensity to adopt innovations such as values and tolerance of ambiguity, is not included in current DOI work; they recommended such literature be linked in the future (Greenhalgh et al. 2005).

The second framework I chose to consider was the PARiHS framework, which was developed by Kitson et al. (1998), refined over time (Rycroft-Malone 2004, 2008a; Rycroft-Malone & Bucknall 2010) and has received much attention from implementation researchers (Conklin & Stolee 2008; Doran & Sidani 2007; Estabrooks
et al. 2007; Helfrich et al. 2010; Helfrich et al. 2009; Meijers et al. 2006; Rycroft-Malone 2008a; Stetler et al. 2011; Wallin et al. 2006). Promoted as a guide for the implementation of CPGs, the framework includes factors that clinicians need to take into account when implementing evidence into practice.

This multidimensional framework proposes that successful implementation involves interplay between three core elements that have their origins in research, quality improvement and practice development; these elements are evidence, context and facilitation (Harvey et al. 2002; Kitson, Harvey & McCormack 1998; Kitson et al. 2008; McCormack et al. 2002; Rycroft-Malone 2004). Each element has several sub-elements with indicators for high and low likelihood of successful change. The authors proposed that successful implementation is dependent on the level and nature of the evidence (high evidence); a context that is receptive to change, with sympathetic cultures, strong leadership, and appropriate evaluative systems (high context); and appropriate facilitation of change, with input from skilled external and internal facilitators (high facilitation) (Kitson, Harvey & McCormack 1998). McCormack et al. (2009) developed the Context Assessment Index to measure these components of context in the workplace. However, the PARiHS framework makes little mention of the role of individual clinicians in this process.

In summary, although there is consensus in the literature that context is vital to practice innovation and best practice the specifics are unclear. Both the model and framework presented here agree that transformational leadership, skilled facilitation, adequate resources and a perceived ‘readiness’ for change are essential factors, but what they should look like is also unclear, as is the role of individuals in the process. The work of the thesis emphasises that the individual characters and their relationships with others are crucial to successful knowledge generation, translation and practice change. Collectively, the physical environment, the nature of the work, the available resources and the individual characters that provide care create the culture within the practice environment. Since implementation science suggests contextual factors are extremely important in research utilisation, and given my understanding of contextual factors in knowledge generation and evidence use, I sought to understand more about workplace culture and determine what constitutes an effective workplace.
7.4 Understanding Workplace Culture

Culture is not just one aspect of the practice environment—it is the practice environment. According to Rycroft-Malone et al. (2004), culture is intrinsic in every workplace and refers to the inherent values and beliefs, roles and relationships, how power is distributed and used, and the resources allocated for implementation of evidence into practice, or simply, ‘the way things are done around here’ (Drennan 1992, p. 3). Culture is shaped by historical, social, political and economic forces but, most importantly, because practice is a social process, culture is social; it is created in every interaction (Wilson, McCormack & Ives 2005). This fact explains why change is so difficult. Cultures vary from organisation to organisation, from hospital to hospital and from ward to ward. Within these, there are cultures within the health professions such as medicine and nursing, each with their own values, belief systems and philosophies. The literature describes the multiple cultures, subcultures or idiocultures within organisations that each have their own agenda and perspective (Bolon & Bolon 1994; McCormack, Manley & Garbett 2004).

The literature convincingly argues for the need to create healthy working environments not only to ensure patient safety but also to keep clinicians safe (Hendrich et al. 2008; Vischer 2008). For many years, Manley has challenged clinicians to assess the effectiveness of their workplace and argued that, while the current focus on organisational change is crucial to enabling local cultures to flourish, it is the workplace culture, the microsystem level, experienced by patients, users and staff that has the major influence in the quality of care provided and in which we should invest (Manley 2004, 2008; Manley 2013; Manley et al. 2011). The work of this thesis supports Manley’s argument; it is imperative that we focus on improving the workplace culture within the NICU as it affects the families’ journey: their experiences, the quality of the care provided and neonatal health outcomes.

In the following section, Manley et al.’s (2011) effective workplace cultures framework identifies key elements that contribute to recognising and enabling an effective workplace culture. Four of the elements included in this framework reflect those within
the DOI model (Greenhalgh et al. 2005) and the PARiHS framework (Kitson, Harvey & McCormack 1998; Rycroft-Malone et al. 2002) mentioned previously; these are transformational leadership, skilled facilitation, availability of resources and ‘readiness’ for change. This framework therefore seems a ‘good fit’ when seeking to identify what constitutes an effective workplace. Manley and colleagues (2011) developed the framework from a rigorous concept analysis based on the principles of practice development methodology that aims to achieve effective workplace cultures that are person-centred. McCormack and McCance (2011, p. 1) defined person-centred care as treating people as individuals, respecting their rights as a person, building mutual trust and understanding, and developing therapeutic relationships.

7.4.1 What an effective workplace culture ‘looks and feels like’

Figure 7 presents the effective workplace culture framework, which includes essential attributes, enabling factors and consequences (Manley et al. 2011). Aspects of this framework are highlighted and discussed below. The framework identifies five attributes of an effective workplace culture. Attribute one—specific values shared in the workplace—identifies ten core values and principles that need to be made explicit.

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within the workplace. These core values are classified in three key domains or clusters: person-centredness, working with others and effective care, as depicted in Figure 8.

![Figure 8: Ten Core Values Classified into Three Key Domains](image)

The framework includes both individual and organisational enabling factors of an effective workplace culture. Individual enablers include the presence of transformational leadership, skilled facilitation and role clarity; organisational enablers include flattened and transparent management, readiness in relation to EBP and cultural change, and a supportive human resource department.

Based on the framework, Manley et al. (2011, p. 17) defined an effective workplace culture as:

A local workplace characterised by the experience of three value sets by all who come into contact with it: a focus on person-centredness, collaborative, inclusive and participative ways of working; and a focus on providing effective care. These values are embedded in local formal systems of evaluation, learning, development and stakeholder participation that reflect and sustain them. Effective workplace cultures are recognised by flourishing of all involved, consistent achievement of standards and goals, evidence-based and continuous development, improvement and innovation in practice linked to the needs of patients, and, empowered and committed staff. These cultures are enabled by transformational leaders, skilled facilitation and role clarity and

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are complemented by organisational readiness with a flattened and transparent management structure and supportive human resource department.

In working through this framework and the literature that informed its development, it became clear why I had found it difficult to implement change (introduction of incubator humidity) and generate new knowledge (pilot study) within my workplace. On reflection, I found none of the enablers or attributes identified by Manley and colleagues as contributing to an effective workplace culture present in my workplace. I admit to being somewhat naive about many contextual issues when I started this work and now have a greater understanding of the multiple factors at play in every practice environment. However, it is still not clear to me how and where to begin with a practice environment that is not in a state of readiness to develop a culture of effectiveness and how we might improve the way that individual characters relate to each other.

The final section of this chapter provides an overview of the context of the intensive care environment and, in particular, my experiences of the context of my workplace. The context of the practice environment includes the physical environment, the nature of the work, the resources (including technology and research evidence) and the characters.

7.5 The Context of Intensive Care
7.5.1 The physical environment, the nature of the work and resources

Complexity is a given for health care professionals working within intensive care environments (Donchin & Seagull 2002; Dong et al. 2012). High stress, high acuity, noise, fast-paced decision making, huge emotional and cognitive burdens, ethical dilemmas, increasingly complex interventions, the unpredictability of the work environment, uncertain patient outcomes and end-of-life care are all in a day’s work for the intensive care clinician (Bucknall 2003; Bucknall & Thomas 1997; Elpern, Covert & Kleinpell 2005). Additional stressors, as highlighted in Chapter Four, affect all health care clinicians and include the challenges of organisational restructuring, shrinking budgets, poor staffing and inappropriate skill mix, time demands, role ambiguity, mandatory overtime, unrealistic workloads, complex relationships and interpersonal
conflicts, poor communication and ineffectual leadership (Duffield et al. 2005; Fischer et al. 2000; Nursing and Midwifery Office 2007; Rosenstein, Russell & Lauve 2002).

Evidence suggests that environmental stressors, in the absence of effective leadership, leave clinicians feeling undervalued, stressed, dissatisfied and burnt out (Braithwaite 2008; Cummings 2011; Garrett & McDaniel 2001; Haward, Kirshenbaum & Campbell 2011; Klopper et al. 2012; Merlani et al. 2011; Oates & Oates 1995; Poncet et al. 2007; Scott et al. 2008) and create an environment that is not conducive to reflective practice or innovation (Apekey et al. 2011). Further, the literature links overtime, working hours and job satisfaction to care rationing and patient outcomes (Aiken et al. 2002; Duffield et al. 2007; Rochefort & Clarke 2010; Twigg et al. 2012). The NICU environment is no exception.

NICUs are an example of where we might expect the workplace characteristics and stressors described above to play out in the extreme. Care of a sick extremely preterm infant is very often more chaotic than the literature describes. Existing evidence and established protocols do not always apply to this group of infants. Further, the treatments that might be possible might not be the right thing to do for individual patients and their families. Decision making in the face of this uncertainty is complex and poses both practical and ethical dilemmas for doctors, nurses and families, especially in relation to the burden of aggressive treatment that prolongs inevitable death rather than prolonging life and in the defining of ‘quality’ of life and best interests (Barnum & Catlin 2009; Moratti 2010; Shewchuk 1995; Spence 2000; Wilkinson 2006).

7.5.2 My workplace

My experiences of the NICU environment mirrored those of other neonatal nurses as revealed in the survey presented in Chapter 4. It became apparent to me that many of the inherent characteristics within my workplace had developed over many years. In my clinical experience, which has more recently been supported by my observations in a state-wide role, NICUs are often co-located with maternity services and situated within adult hospitals. Arguably, the NICU is invisible within an adult hospital and, therefore,
runs the risk of being viewed as different or insular, and perhaps marginalised in relation to the organisation’s priorities. Working in isolation affords little opportunity to network, to develop communities of practice or to develop leaders with ‘big picture’ knowledge. This has the potential to limit individual clinicians, the care they provide and the NICU’s ability to cope with change.

The workplace functioned in a medical model where rigid hierarchical control reigned supreme and practice was based on local experience, tradition and practitioner preference. Practice regularly changed shift by shift depending on the physician on call, there was no consensus on a multitude of therapies. Participants in the survey of humidification practices (Chapter 4) reported similar inconsistencies. The existing culture in my workplace, rather than available research evidence, therefore dictated how the work was done; there was no open enquiry, no evaluation of existing practices or of possible alternatives. An example of where groupthink (Hart 1994; Janis 1972, 1982) is dangerous.

From my experience of the practice environment and analysis of the data from the survey (Chapter 4) and the single-centre audit (Chapter 5), nurses appeared invisible in this clinical context especially as thermal management and fluid balance, and therefore, incubator humidity, is considered practices within the nursing domain. Confronted with the uncertainty and ambiguity associated with care practices, decision making, and patient outcomes, it appears that nurses resorted to routines, rituals and task-focused care that passed from one generation to the next. Greenwood suggested that routine practices protect nurses from the risks associated with individualised clinical decisions (Greenwood et al. 2000). Routines seemed to reduce the tension and stress created by interpersonal conflict with individuals whom they perceived had power over them through either status or expertise; nurses adopted a passive approach, followed medical orders and obeyed commands without question to ‘fit in’ with the environment. Scott et al. (2008) described nurses retreating to a zone of safety in uncertain contexts; Vaismoradi, Salsali and Ahmadi (2011) termed this behaviour as avoiding trouble. Such workplace dynamics are congruent with those reported by Menzies (1960) in her work titled ‘Social Systems as a Defense against Anxiety’. Sadly, it would appear that little has changed since that time.
Nurses in my workplace were always busy, and had no apparent time to reflect on practice or to consider alternative ways of doing things. The literature describes this culture of busyness in nursing (Manias & Street 2000; Manley 2008; Martin 1998; Scott-Findlay & Golden-Biddle 2005; Thompson et al. 2008; Wilson, McCormack & Ives 2005). Schein (1992) postulated two extremes of how work is construed and valued: a ‘doing’ or a ‘being’ culture. Scott-Findlay and Golden-Biddle (2005) observed that acute care nurses’ work has a focus on ‘doing’—on completing tasks—which is highly regarded and perpetuated by practitioners, administration and the public. The authors suggested there is tension between the ‘doing’ and the need for ‘being’ (reflecting, reading, education). Further, Martin (1998) proposed that nurses use busyness to shield themselves from emotional involvement and potentially painful experiences. Thompson et al. (2008) concurred and suggested the mental time and energy required to navigate complex environments and a culture of busyness more accurately reflect what may be meant by ‘lack of time’ as a barrier to research utilisation.

Protective of the infants in their care, nurses became gatekeepers rather than advocates who, with the best intentions, presented a barrier to families, research endeavours, innovation and practice change. The literature describes similar ‘overprotective’ behaviour (Sandberg et al. 2002; Scott & Pollock 2008; Wielenga, Smit & Unk 2006). Anything (or anyone) that challenged the status quo in this clinical context was unwelcome and perceived as threatening. However, change was inevitable.

Despite the rhetoric that management styles are changing and transformational leadership, which enhances the motivation, morale and performance of clinicians, is now the norm, the reality for many clinicians is quite different (NSW Government 2013). I witnessed disruptive and discriminative behaviour, bullying and the social exclusion of individuals outside previously established cliques that created a toxic work environment that reduced morale and negatively affected the quality of patient care. Martin (2008) and Salin (2003) proposed that toxic workplaces occur as a result of managerialism and micromanagement, with management style considered a contributor to clinician stress, dissatisfaction and staff turnover (Rosenstein 2002). The literature is
littered with similar examples of toxic workplaces (Aasland et al. 2010; Holloway & Kusy 2011; Holloway & Kusy 2010; Hutchinson et al. 2006; Hutchinson et al. 2009; Johnson & Rea 2009; McAvoy & Murtagh 2003; Padilla, Hogan & Kaiser 2007; Quine 2001). The behaviours I witnessed are analogous to the oppressed group behavior described by Roberts (Roberts, Demarco & Griffin 2009) and the literature has also previously described this nurse-to-nurse bullying (Bartholomew 2006; Woelfle & McCaffrey 2007). It seemed to me that, within my workplace, not only patient care but also the psychological safety of staff was under threat. Change however was inevitable.

Change arrived in the NICU as worldwide attention focused on the effect of the physical environment on extremely preterm infants (Graven & Browne 2008b; Laudert et al. 2007). Since their inception, NICUs have become large, bright, noisy, highly technical units housing large numbers of infants. Previous recommendations for NICU design emphasised cleanliness and efficiency, but neglected the potential effect of the NICU environment on preterm infants (White 2004, 2005). The growing understanding of the substantial effect of sensory input on the developing brain, recognition of the need to create an individualised microenvironment based on specific needs and the advent of developmentally sensitive interventions (Als et al. 2003; Bhutta & Anand 2002; Browne 2011; Browne & White 2011; Graven & Browne 2008c; Peters et al. 2009) provided the impetus for change within NICUs that included redesign (Altimier 2004; Carlson et al. 2006; Domanico et al. 2010; Floyd 2005; Laudert et al. 2007; McGrath 2005; Milford, Zapalo & Davis 2008; Peng et al. 2009; Pineda et al. 2012; Shahheidari & Homer 2012; Shepley 2004; Stevens et al. 2012; Stichler 2012) and massive mobilisation of resources.

Consequently, the tailoring of the NICU environment to meet the developmental (particularly neurological) requirements of extremely preterm infants has led to the evolution of physical environments and care practices that work with rather than against these requirements. These changes in the NICU far outpaced even the major changes that occurred in the overall hospital environment in the same period (White 2005) and involved a move from large open ward areas to single (or two-bed) rooms. The assumptions behind this initiative was that such environmental modifications would decrease sensory stimulation by reducing noise, lighting and the unnecessary handling
of infants and thus promote physiologic stability (Graven & Browne 2008a, 2008b, 2008c).

It is too early to say whether the modifications to the physical environment of the NICU will translate into improved health outcomes. Evaluations to date have been variable (Inder 2013; Pineda et al. 2012; Walsh, McCullough & White 2006). Improving the family focus of care provision is a positive outcome of the changes, but the modifications appear to have brought about new challenges. Some parents found single-patient rooms more stressful than open units (Pineda et al. 2012), and clinicians described increased stress, the need for additional staffing and social isolation following unit modifications (Walsh, McCullough & White 2006). Of greatest concern, these newly created environments may not have had the intended effects on extremely preterm infants. Preliminary work by Inder (2013), which used neuroimaging as a window into the newborn brain to evaluate the nature and timing of injury and alterations in brain development, suggests the NICU with single-patient rooms may not provide sufficient stimulus for healthy neurodevelopment. Further research is required to determine the optimal environment for extremely preterm infants; this of course includes the optimal microenvironment within the incubator. However, changing the physical environment does not necessarily change the way clinicians work.

### 7.5.3 The characters

The characters, or myriad of clinicians or professional groups, determine the nature of a practice in any given context. My work suggests that the characters and their relationships with others have the biggest effect on the culture of the workplace and the care provided. The characters perceived as having the power to direct care influenced humidification practices on a day-by-day, shift-by-shift basis, causing inconsistency in patient care, and uncertainty and frustration for other clinicians and parents, as evidenced by the findings of the survey (Chapter 4). Because individuals react to the environment in which they find themselves, their behaviour affects how others behave as well. Nurses obeyed commands even when they believed the intervention was not in the patient’s best interests, and had the potential to create ethical and moral dilemmas (Ahlström et al. 2008; Elpern, Covert & Kleinpell 2005; Garel et al. 2011; Hefferman &
Heilig 1999; Pauly et al. 2009). The behaviour of individual characters also influenced the design of the multicentre trial and the conduct of the pilot study.

Teamwork is at the heart of NICU practice. It is generally accepted that not all members of the team are equal—someone, usually the medical consultant, is ultimately responsible for decision making—but to optimise patient care, it is crucial that team members work together well (Beckett & Kipnis 2009; Bower et al. 2003; Davenport et al. 2007; Garling 2008; Lemieux-Charles & McGuire 2006; NSW Department of Health 2008; Schmitt 2001). A wealth of literature describes teamwork and how to ensure the team works effectively. Although evidence suggests that effective teamwork improves the quality of care, increases patient safety, reduces workload and burnout (Clements & Helmer 2006) and creates greater job satisfaction (Kalisch, Lee & Rochman 2010) and despite some published successes, in general, the solution to improving workplace relationships in health care has largely remained elusive, and autocratic leaders and hierarchical structures prevail. Mann (2004) suggested that mutual respect should be a primary goal in teamwork, regardless of position, status or authority. However, in his inquiry into the Acute Care Services in NSW Public Hospitals, Garling (2008, p. 22) found ‘the culture endemic in NSW Health, which has been around for a very long time, is an unhealthy one … respect is an essential but absent value’.

When teamwork and communication are ineffective, clinical care is impaired and errors occur (Alvarez & Coiera 2006; Kohn, Corrigan & Donald 2000; Kugelman et al. 2008; Murphy & Dunn 2010; NSW Department of Health 2009, 2011; O’Leary et al. 2010; Patterson et al. 2004; Reader, Flin & Cuthbertson 2007; Sharek et al. 2006; Snijders et al. 2007). In a series of studies, Rosenstein and colleagues reported the negative effect of disruptive clinician behaviour on patient outcomes in perioperative areas (Rosenstein & O’Daniel 2006), operating theatres (Rosenstein & O’Daniel 2008), obstetrics (Rosenstein 2011a) and emergency departments (Rosenstein & Naylor 2012); they proposed that it is time to hold individuals accountable for their behaviour and identified the need for support and training to improve communication and team collaboration (Rosenstein 2011b). These studies suggest relationship issues are prevalent across health care environments. Acknowledging this, and with a view to addressing such issues within the practice environment, the American College of
Physician Executives recently published a white paper titled *Disruptive Physician Behaviour* (MacDonald 2011).

These studies suggest that health care struggles to optimise its largest and most valuable resource: the characters that provide patient care. While many disciplines contribute to neonatal care provision, the relationship between nurses and doctors continues to cause the greatest concern (Fagin & Garelick 2004; Gjerberg & Kjølsrød 2001; Krogstad, Hofoss & Hjortdahl 2004). This is not a surprise finding for three reasons. First, nurses and doctors work very closely together in the NICU environment. Second, neither existing nursing and medical curriculum nor subsequent training equips clinicians with the tools necessary to deal with the complex relationships that exist in such intensive and demanding environments. Evidence of this is the high number of education, team building, conflict resolution, and leadership and management courses continually funded by health care aimed at changing behaviour to address ongoing relationship issues. Third, despite the many improvements described in contemporary health care in general, there is evidence that the doctor–nurse game first described by Stein (1967) is still being played today (Joint Commission 2008; Stein, Watts & Howell 1990).

A plethora of literature attests to the conflict between doctors and nurses over time and the atmosphere this tension creates within the workplace (Chaboyer & Patterson 2001; Curtis, Tzannes & Rudge 2011; Devine 1978; Fagin 1992; Fagin & Garelick 2004; Krogstad, Hofoss & Hjortdahl 2004; Radeliffe 2000; Schmalenberg & Kramer 2009; Stein, Watts & Howell 1990; Tellis-Nayak & Tellis-Nayak 1984). This conflict finds its basis in the cultural underpinnings of the two disciplines, whose divisions are rooted in education, gender and income. Historical and time-honoured traditions of medicine and nursing including gender inequalities have caused the issues to become deeply entrenched in the male-dominated and administrative cultures of hospitals, in which nursing is viewed as a subservient role and disruptive physician behaviour is tolerated (Gordon 2005; Rosenstein 2002). The profession gives doctors implicit power based on education and social status—privileges that even the most junior doctors possess, and that are often abused (Joint Commission 2008) with negative consequences for individuals, the team and patient safety (Burke et al. 2006; Gordon 2005; Nembhard & Edmonson 2006; Nugus et al. 2010; Rosenstein 2002). Nugus et al. (2010) observed
that this caste system persists today and posits that the effects of this hierarchical system are not to be underestimated.

Crawford, Omery and Seago (2012) described nurse–physician communication as an ongoing conundrum. The authors concluded that differing world views, poor collaboration and communication, and power struggles cause dysfunctional interpersonal relations that are associated with clinical errors, inefficient care delivery and frustration. Innovations that challenge existing practices provoke emotion, and role changes can engender fear of relinquishing professional turf; the challenges of implementing the nurse practitioner role are evidence of this (Clements & Helmer 2006; Foster 2010). In her recently published PhD thesis investigating interpersonal relationships in the NICU, Dunn (2011) described the need to buffer power differentials to optimise decision making and patient care. The Garling Report posed that ‘the rigid demarcation between what a doctor’s job is, and what a nurse’s job is, needs to be consigned to history’ (Garling 2008, p. 3). Nurses and doctors need each other to provide patient care, and given the current focus on optimising neonatal care worldwide, the need to increase both individual and team effectiveness in NICUs has never been greater.

During the years of undertaking this thesis, I have witnessed the effects of the workplace culture on individuals over time. My experience of practice environments that do not have the attributes required to function effectively, as proposed by Manley et al. 2011) can have devastating effects; they can destroy people. The published literature echoes these experiences (Cusack 2000; Patole 2002; Vickers 2004). Individuals are traumatised physically and psychologically by toxic workplaces to the extent that, in coming to terms with what is occurring, they develop coping mechanisms and survival strategies that limit them both as clinicians and as human beings (Vickers 2004). If the basic human needs of clinicians are not met, it is not surprising that clinicians fail to meet the basic needs of patients and families in their care. Patterns of behaviour evolve and practices become habits that often go unchallenged. Clinicians may deny uncertainty because to question existing practice might mean accepting uncertainty and that has enormous implications; the possibility that the care provided may not be optimal might be a concept too overwhelming to consider.

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There is a pressing need to address workplace cultures within health care. Some of the issues raised here might unsettle entrenched beliefs. However, we have an ethical and moral imperative to understand social norms, and to focus on utilising the strengths of individual clinicians rather than fear and enable workplace effectiveness. Effective workplaces that embrace and effect change are those that have a culture of creativity and innovation, have strong transformational leadership, skilled facilitation and relatively flat hierarchical systems. This is in contrast to hierarchical models within health care systems and professional groups. Enabling effective workplace cultures could have tremendous public benefit by improving both patient and clinician health and wellbeing, and reducing health care costs. Raising awareness of the need for change is an important first step.

7.6 Chapter Summary

In this chapter, I reflected on my doctoral journey, the major findings and the decisions made. The work revealed the complexity of the NICU context and the real life challenges of working in inhospitable contexts. Discussion revealed factors that comprise context: the physical environment, the nature of the work, the availability and use of resources and the individual characters that provide the work. The context within any given environment creates the workplace culture—and the culture within the workplace determines how the work is done. To improve patient care it is essential to seek ways to enable the development of effective workplace cultures, a challenge for all health care professionals.

7.7 Where to from Here?

Health care has invested significant amounts of time, energy and resources on attempts to engage clinicians to improve patient outcomes. In fact, whole departments and ongoing reforms are dedicated to translational research (NHMRC 2012). However, during this research journey, I have come to believe that political agendas, organisational and management decisions, and research evidence will never influence patient care at the bedside in the way they are intended until we find ways to improve
relationships within the practice environment. The work of this thesis suggests it is the
individuals—the behaviour of the characters within the workplace—that determine the
context, how they interact with others and how patient care is provided. ‘Working with
others’ is a key domain of the effective workplace cultures framework that highlights
the importance of relationships and teamwork to an effective workplace. In addition,
attributes within this framework have been recognised as contributing to successful
implementation of an innovation (Greenhalgh et al. 2005; Kitson, Harvey &
McCormack 1998; Kitson et al. 2008; Rycroft-Malone et al. 2002). Therefore, it is
reasonable to expect that any attempts to change the way that care is provided must first
focus on the individual characters. Models that report a positive effect on patient care
have one thing in common: they link people together (Adewale et al. 2007; Cummings
et al. 2007; Gittell, Seidner & Wimbush 2010). So perhaps the greater question to ask is
‘what drives social processes and human behaviour?’

How then do we find a way forward that pays due attention to health care’s most
valuable asset—the people? Perhaps we need to view the dilemma in a new and very
different way. If individuals and their relationships are so important, we need to know
much more about the imperatives at play for both individuals and their relationships.
Perhaps we should first meet the fundamental needs of the individual clinician. For
person-centred care to occur, we first need to develop person-centred cultures within the
practice environment. Why not invest in an individualised person-centred approach to
clinicians that meets their basic needs and is based on contemporary evidence? If we
work creatively with the realities of human nature and meet the needs of individual
clinicians rather than attempt to change or ignore them, which in essence might prove
much simpler, working with the evidence to improve patient outcomes may become a
less onerous task.

Using the work from contemporary neuroscience and neuroleadership, the final chapter
suggests a reasonable way forward that can change these all-important interactions and
has the potential to improve relationships, workplace culture and ultimately patient care.
Chapter 8: C’ing a Way Forward: the Complexity of Working as, and with, Human Beings, Seeking to Build Healthier Relationships

8.1 Preamble

Most of us who work in neonatal paediatrics are distressingly familiar with the sight of a small infant surrounded by a fog of vapour within a closed tent or incubator. This situation perhaps symbolises the present status of this subject, which is essentially a very small body of facts enveloped in a misty atmosphere of speculation, which is walled off from its surroundings by a rigid container of prejudice. (Clement Smith 1955, p. 2051)

At the end of my doctoral journey, I find myself reflecting on the same quote that was clearly a part of its commencement. However, this time I am driven by a different, more fundamental set of questions concerning the NICU context and ways forward for enhancing the culture to enable more person-centred and effective processes and outcomes—for all. Therefore, instead of positioning the fragile premature infant within the rigid container surrounded by fog, I am using the analogy to expose and explore the reality of the ‘NICU container’ for the clinicians who seek to provide the best possible care for infants and their families. The circumstances and challenges that shaped my doctoral journey, and generated the knowledge and learning contained within this thesis, took me away from my initial questions concerning humidification practices. I found myself engaged in the explication of broader and more basic questions related to the social processes that are at the centre of complex workplaces in which human beings seek to engage in the highly emotive, often distressing and always dynamic social processes that are part of the NICU landscape. Therefore, within this final chapter, I seek to outline and integrate two fields of endeavour: social, cognitive, affective neuroscience and its application to workplaces; and approaches to engaging staff and enabling the transformation of individuals, practices and the workplace culture itself to be more person centred, effective and self-sustaining. As Machiavelli (2007 [1515]) observed:

It ought to be remembered that there is nothing more difficult to take in hand, more perilous to conduct, or more uncertain in its success, than to take the lead in the introduction of a new order of things. Because the innovator has for
enemies all those who have done well under the old conditions and lukewarm defenders in those who may do well under the new.

8.2 Chapter Overview

In a chapter that highlights the importance of emotion in human behaviour and healthy, collaborative relationships in the workplace, it may seem strange that I have chosen to begin with a quotation from Machiavelli. Machiavelli’s ideas denote his propensity to be unemotional, engage in amoral manipulation, distrust and seek to control others, and pursue status for himself (Dahling, Whitaker & Levy 2009). Indeed, Machiavellianism is viewed as one of the constituents of the ‘dark triad’: Machiavellianism, narcissism and psychopathy (Paulhus & Williams 2002). I have not included this quotation because I believe Machiavellian attributes are something to which we should aspire. Rather, I include it because of its strong resonance with my experiences of the change process with which I have been involved, and it describes perfectly some of the behaviours that I witnessed in my workplace and highlighted in this work. Alternatively, it may simply reflect my yearning for a workplace where rational and powerful leadership is able to ‘take care of business’ such that the complexity and uncertainty are dealt with and everyone can focus on providing safe and high-quality care to the infants and their families.

In lieu of the likelihood that all-powerful leaders are going to (or would even be able to) come to our rescue, this final chapter asks the ‘where to from here?’ question. The previous chapter outlined my understanding of the elements that comprise the NICU context and the attributes of an effective workplace culture, together with the major findings of the thesis. This outline made clear the central role of the health care professionals themselves (characters)—in creating the physical environment, influencing the nature of the work and determining the ways in which practice evolves, including resource and research evidence utilisation. Consequently, in this chapter, I seek to explore some fundamental drivers of social processes and human behaviour within complex workplaces as a means of identifying potential ways of influencing change that might lead to more positive and engaging workplaces.
In this chapter, I introduce the reader to contemporary neuroscience—a discipline that explores the biological foundations of the way humans relate to each other and to themselves—and to an emerging field of study known as neuroleadership (NeuroLeadership Institute 2013) that connects neuroscientific knowledge with the fields of leadership development, management training and change management, consulting and coaching. The chapter reveals how these disciplines show promise, seem reasonable approaches, and may hold the key to helping us understand both individual needs and workplace relationships that have the potential to help us to move forward through the complexity of today’s health care system. Currently, there is a dearth of strategies for transforming workplace cultures (Manley, Crisp & Moss 2011).

In this chapter I offer a way forward—a new order of things (as Machiavelli would say) that has the potential to increase staff engagement, improve relationships and enable the creation of effective workplace cultures. I begin by acknowledging practice as a social process and emphasise the need to understand more about social relationships in the workplace. I then consider the social brain and introduce the work of contemporary social, cognitive, affective neuroscience to gain insight into human behaviour. Next, I explore the five social domains of basic human needs captured within the SCARF model (status, certainty, autonomy, relatedness and fairness) (Rock 2008; Rock & Cox 2012) and briefly explore what that model suggests in relation to improving staff engagement and performance in complex clinical environments. I then reflect on the work of the thesis, the discoveries made and the way forward proposed. Finally, to conclude, I revisit the concept of certainty, as this is where the work began, with my desire to seek certainty around the use of incubator humidity in the care of preterm infants.

8.3 Practice as a Social Process

Contemplate the NICU environment—to those who walk into the NICU today, it gives the impression of an environment that is almost futuristic and highly technical, and has, as Mesman (2008, p. 1) described, ‘a strange sense of order’. This is the ‘doing’ part of practice visible to the outsider. However, what lies beneath is much more complex and goes much deeper. As I write this, I am reminded of Fish and Coles’ (1998) iceberg.
The authors used an iceberg as a metaphor for professional practice. The part of the iceberg above the waterline is explicit and visible to all (for example, tasks, tools, processes); in contrast, the larger part that lies below the waterline is not visible but is, nevertheless, essential for its stability. According to Fish and Coles, this world below the waterline that is hidden from view represents individuals’ experiences, feelings, expectations, assumptions, fears, values and belief systems. Efforts to improve patient care by increasing research use have primarily targeted acts of ‘doing’: the visible, the explicit, and the interventions that occur above the waterline. This does not only apply to health care organisations. In an evaluation of a decade of organisation development efforts, van Eijnatten and van Galen (2002) reported that ‘exterior’ aspects of the system such as tasks, structures, tools and technology had received the most attention, while ‘interior’ aspects such as individuals’ thoughts, beliefs and feelings had been virtually ignored. As clinicians, we like to believe we can make decisions logically and rationally. However, in a thought-provoking book, neurologist and novelist Robert Burton (2008) proposes that our thoughts are based on emotions and are largely unconscious. That an understanding of human cognition requires the consideration of emotion is not a new concept (Phelps 2006).

Perhaps, then, it is time to change our thinking. Rock (2006) proposes that thinking occurs at the base of the iceberg—that what we achieve at work is driven by how we think. To improve performance, we must start at the bottom—actually improve our thinking. Perhaps it is time to reveal what lies beneath that which is visible—the implicit—uncomfortable though that may be. Perhaps it is time to focus on the fundamental needs of those seeking to provide the best care possible to preterm infants and their families. One potential way forward, in mitigating the effect of the contextual challenges (the complex nature of the work and the workplace), is to work with the ways in which the realities of the human brain influence performance and engagement with our work and affect the fundamental relationships that make our work possible. The field of contemporary neuroscience points to the realities surrounding intrapersonal and interpersonal processes and their effect on the social processes at the level of care provision. What are the implications for practice in NICUs if we look through the lens of neuroscience? In the following section, I seek to understand the brain at work and establish how this knowledge might improve relationships in the workplace.
8.4 Considering the Social Brain

Social cognitive affective neuroscience (SCAN) is an evolving field of interdisciplinary research combining knowledge of social science disciplines (specifically, social psychology) and cognitive neuroscience to address questions about the mechanisms underlying emotion–cognition interactions (Ochsner & Gross 2008). The field brings together questions related to the social (motivational and social factors relevant for behaviour and experience), cognitive (information-processing mechanisms) and neural (brain mechanisms) processes (Ochsner 2007; Ochsner & Lieberman 2001). This approach focuses on social phenomena, such as the representation of the minds of others, empathy, agency, reflection of one’s own experiences, emotions, the self as part of the social world and social decision making (fairness, trust and cooperation) using traditional neuroscience methods and tools such as neuroimaging and neuropsychology (Lieberman 2007).

The use of brain imaging technologies for the investigation of social phenomena is new. Imaging technologies such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), along with brain wave analysis technologies such as quantitative electroencephalography (qEEG) and transcranial magnetic stimulation (TMS), have revealed previously unseen neural connections in the living human brain (Harrison & Ross 2010; Senior, Lee & Butler 2011). Theoretically, a link exists between the brain (the physical organ) and the mind (the human consciousness that thinks, feels, acts and perceives), and through advanced computer analyses of these connections, a new body of knowledge is evolving. Together with the measurement of neurotransmitters, neuroimaging can demonstrate what happens in the brain during stressful emotional states.

Our brain deeply hardwires the things we do at work every day; thus, they are habitual. Our habits are unconscious to us; we do not ‘have in mind’ what we are doing in our working memory. Rock (2006) indicated that, once we have done a job for some time, we are unconscious for much of our workday—a concept coined by philosopher Adam Smith as ‘the impartial spectator’ (Debes 2012). Rock took this concept a step further
and postulated that capacity for change might be determined by how well individuals know their brains and their capacity to consciously intervene in otherwise automatic processes (Rock 2009). Contemporary neuroscience based on studies of healthy and diseased brains suggests that the brain retains its plasticity throughout life and thus has the capability to change the nature of electrical activity and make new neuronal connections (Johansson 2004). This finding suggests to us that, with focused attention, even the most entrenched behaviours can change (Rock 2008). Business executives, athletes and military leaders have already begun to explore various brain science applications in seeking to optimise performance (Waldman, Balthazard & Peterson 2011). Perhaps ‘training’ the brain of clinicians to improve communication, collaboration, interpersonal relationships and performance is also possible and worthy of consideration.

Two emergent themes from the SCAN literature are, first, that motivation to minimise threats and maximise rewards drives social behaviour (Gordon 2000), and second, that many of the domains of the social experience use the same brain networks to minimise threat and maximise reward as those used for primary survival needs (Lieberman & Eisenberger 2008). What this means is that the brain responds to social needs and situations in the same way as it responds to basic needs such as breathing, food and water. Humans have a fundamental need to belong, are incredibly sensitive to their social context, and are strongly motivated to remain in good standing with their social group and avoid social exclusion (Heatherton 2011). Thus, SCAN proposes that social needs do not belong in the middle of the five-level hierarchy of needs depicted by Maslow’s (1943) theory of motivation, but rather are more fundamental, more crucial to our wellbeing—that they actually belong at its base: the biological or physiological level (Lieberman 2007).

The minimise threat/maximise reward response is similar to the approach-avoid response essential for survival that recognises what is good or bad in the environment (Amaral 2003). The amygdala within the limbic system plays a central role; its actions are reflexive, not under conscious control, and are proportionate to the intensity of the emotional response (Amaral 2003; Amaral et al. 2003; Dolan 2007). Once a threat or avoid response is perceived, there is a decrease in the resources available to the
prefrontal cortex (Arnsten 1998; Ohman 2005; Zaretsky et al. 2010). The consequence is a reduction in oxygen and glucose available for functions involved in working memory and problem solving (Subramaniam et al. 2009; Zaretsky et al. 2010). This explains why we are unable to think clearly, when someone threatens our status. An activated amygdala causes overgeneralisations, risk avoidance, defensive actions and small stressors to be perceived as major ones (Phelps 2006), and it is more responsive to the threat/avoid response than the reward/approach response (Baumeister et al. 2001). ‘Bad is therefore stronger than good’ because our brain intrinsically focuses on threatening stimuli. If disruptions in the social environment block information to our higher cognitive process and affect higher order thinking (Baumeister, Twenge & Nuss 2002), learning, creativity and innovation are impeded. Further cognitive psychology studies provide clinical evidence that stress, boredom, confusion, low motivation and anxiety can, individually and more profoundly in combination, interfere with learning (Chistianson 1992).

Alternatively, a reward/approach response activates the primary reward neural circuitry, the corticostriatal regions, particularly the ventral striatum, which increases dopamine levels, is involved in affective and motivational processes and suggests engagement (Rock 2008). This is linked to positive emotions, and a willingness to take risks and solve problems, and improve performance (Fredrickson 2001).

The business literature also illustrates the importance of satisfying basic human needs. Harter reported on what is probably the largest series of studies (Gallup) investigating the effects of the workplace environment on employees’ wellbeing and performance (Harter, Schmidt & Keyes 2002). The report included 7,939 businesses and feedback from 198,514 respondents. Satisfying basic human needs, which included clarifying desired outcomes and increasing opportunity for individual fulfilment and growth, was associated with higher productivity and lower rates of turnover. Consequently, knowledge of the drivers of human behaviour and an understanding of how we behave in specific social situations might positively affect our performance—how we lead, manage, collaborate with and influence others in the workplace. Knowledge of the brain’s response to social needs has influenced those interested in promoting leadership
behaviours and the development of a new and exciting field called neuroleadership (NeuroLeadership Institute 2013).

Neuroleadership studies leadership through the lens of SCAN to explore the key elements of self-awareness, awareness of others, insight, decision making and influencing (Rock & Ringleb 2009). In 2008, David Rock, co-founder of the NeuroLeadership Institute, developed SCARF®, a brain-based model for collaborating with and influencing others (Rock 2008; Rock & Cox 2012). This conceptual model aims to improve our capacity to understand and ultimately modify our own and other people’s behaviour in social situations to be more adaptive. Modifying our own behaviour is infinitely more challenging because our social awareness circuitry is far more developed than our self-awareness circuitry (Biesanz et al. 2011); this explains why our first impressions of others are fairly accurate. The brain also uses different brain processes for decision making, depending on the demands of the social environment (Jenkins & Mitchell 2010).

The SCARF® model synchronises new findings about the physiology of the brain (threat/reward principle and primary survival needs) with leadership behaviours within a framework that captures the five domains of human social experience that can affect a social situation, be it threatening or rewarding, and how this manifests in observable behaviour. These domains are status, certainty, autonomy, relatedness and fairness (Rock 2008). Further development of the model expands to explore interactions between the domains and considers individual and organisational differences in SCARF® responses (Rock & Cox 2012). The model’s goal is to help minimise the easily activated threat responses and maximise positive, engaged states of mind during attempts to collaborate with and influence others (Rock 2008). The following section discusses each of the five domains of the SCARF® conceptual model using contemporary evidence from SCAN to understand behaviour in the workplace and suggests how relationships might be improved.
8.5 SCARF®: A Brain-Based Approach to Practice

Figure 9 depicts the SCARF® model (Rock 2008). The following section defines each of the domains within the SCARF® model using evidence from SCAN.

8.5.1 Status

*One’s sense of importance relative to others (e.g. peers, friends, co-workers, supervisors)*

Status is about relative importance, ‘pecking order’ and seniority, and is probably the most significant driver in humans (Zink et al. 2008). According to Marmot (2007), status is the most significant determinant of human longevity and health, even controlling for education and income. Humans are acutely sensitive to social status—that is, their importance relative to others—and tend to be accurate judges of where they fall on the social ladder (Srivastava & Anderson 2011). Further highlighting the importance of status in threat, reward and social processing is the fact that a social or status reward (such as knowledge of a good reputation) elicits a similar response to receiving a monetary reward (Izuma 2012; Izuma, Saito & Sadato 2008).

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1 David Rock granted permission to reproduce this figure.
Status rewards, especially when made public, are deeply rewarding. Similarly, acknowledgement of learning and development also activates the reward circuitry (Mitchell, Macrae & Banaji 2006). This reputation-based decision making drives many aspects of human social behaviour and engages not only the striatum but also the medial prefrontal cortex, the temporal parietal junction and the amygdala (Izuma 2012). This means that the perception of a potential or real reduction in status can also generate a strong threat response and that someone who highly values status may be more likely to react to status-threatening situations in an aggressive and confrontational manner. An aroused threat response inhibits performance and wellbeing (Hambrick & Meinz 2011), especially if individuals consider themselves of lower status than colleagues in the group (Stellar et al. 2012). In addition, seeking a higher status than others reduces relatedness.

The level of status individuals feel within their group is more important to happiness than socioeconomic status (Anderson et al. 2012). Individuals who consider themselves to have high status listen to and place greater value on information from higher status individuals; however, those who consider themselves lower status listen to and value information from both higher and lower status individuals (Ly et al. 2011). Further, people of higher status read the emotions of others less well (Ly et al. 2011). The consequences of perceived low status include reduced cognitive capacity (lower IQ), increased amygdala response and decreased prefrontal cortex response relative to higher group status (Kishida et al. 2012). Further, the brain perceives a reduction in status or social pain from being left out of an activity or group in much the same way as it perceives physical pain; similar circuitry is used (Eisenberger 2012; Eisenberger & Lieberman 2004; Lieberman & Eisenberger 2008). Consequently, social rejection or ostracism can increase inflammatory processes (Slavich et al. 2010) and adversely affect mental health (Williams & Nida 2011). This work suggests the need for inclusion to reduce status threats.
8.5.2 Certainty

*One’s need for clarity and the ability to make accurate predictions about the future*

Humans do not like uncertainty; at best, it makes them feel uncomfortable (Fields 2011). The reason for not liking uncertainty is that the brain is a pattern-recognition machine that constantly tries to predict the future, to ‘know’ the pattern occurring from moment to moment; it craves clarity and certainty so that prediction is possible (Rock 2008). When prediction is not possible, this generates uncertainty; the brain perceives it as an error, which involves the more energy-intensive prefrontal cortex to process the experience. Hedden and Gabrieli (2006) noted that attention focuses on the error until it is resolved, this moves attention away from work goals. Great uncertainties, such as not knowing the boss’s expectations, or experiencing significant change or an ambiguous social situation, can cause significant stress and can be overwhelming and highly debilitating (Ford & Collins 2010). Those individuals with a hypersensitive need for certainty make quick, firm and prejudiced judgements and decisions to reduce ambiguity, and they are more prone to rely on the most obvious and easily accessible information, favour authority and social norms, and stick to their decisions even in the face of new, contradictory information (Roets & Van Hiel 2011). Alternatively, the act of creating increased or even anticipated certainty increases activation in the reward circuitry (Bromberg-Martin & Hikosaka 2009). This finding suggests that, although there is uncertainty in the practice environment, increasing a sense of certainty in others is possible to reduce certainty threats.

8.5.3 Autonomy

*A sense of control over the events in one’s life and the perception that one’s behaviour has an effect on the outcomes of a situation (e.g. obtaining a promotion, finding a partner)*

Humans also have a fundamental need for personal control (Kay et al. 2009). The perception of having autonomy—that is, a need to have control over life events—increases wellbeing and cognitive functioning and improves health (Diener et al. 2010). Psychological prosperity (such as a sense of autonomy), as opposed to economic prosperity, better predicts feelings of wellbeing (Diener et al. 2010; Izuma, Saito &
Sadato 2008; Lee & Reeve 2012; Murayama et al. 2010; Saxe & Haushofer 2008) and job satisfaction (Wood & de Menezes 2011; Wood et al. 2012). Providing significant autonomy in health care is difficult because being part of a multidisciplinary team inherently reduces autonomy. However, with the knowledge that being part of a social system is rewarding, creating a healthy workplace culture that increases status, certainty and relatedness could counteract potential autonomy threats. Even in a highly stressful environment, if a degree of control exists, stress has much less of a negative effect (Donny, Bigelow & Walsh 2006; Dworkin, Mirkis & Smith 1995).

Work by Inesi and colleagues (2011) demonstrated that power and choice are interchangeable. When individuals lack a sense of power (i.e. control over what other people do), they seek out a sense of choice (i.e. control over our own outcomes), and vice versa. We can be content with either a sense of power or a sense of control, or both, but having neither power nor control leads to dissatisfaction and associated social pain. Further, the authors found that power and choice exhibited a ‘threshold effect’—once an individual had one source of autonomy or control, additions of the other source yielded diminishing returns. Taking this a step further, Leotti and Delgado (2011) found that even the opportunity to exercise control or the anticipation of having a choice was inherently rewarding.

8.5.4 Relatedness

One’s sense of connection to and security with another person (e.g. whether someone is perceived as similar or dissimilar to oneself, a friend or foe)

Relatedness is a sense of belonging that makes humans feel good. Cacioppo and Patrick (2008) described the need for safe human contact as being as fundamental as the need for food and water. Even a minimal social connection increases motivation and connectedness (Walton et al. 2012), and having stronger social relationships can prolong life (Holt-Lunstad, Smith & Layton 2010; Shirom et al. 2011). Relatedness involves deciding whether others are ‘in’ or ‘out’ of a social group—whether someone is friend or foe. Meeting someone unknown tends to generate an automatic threat response, and the decision whether someone is friend or foe happens quickly and affects brain functioning (Pelphrey & Carter 2008). For example, information from people
perceived as ‘like us’ is processed using similar circuits for thinking one’s own thoughts. When someone is perceived as a foe, different neural circuits are used (Jenkins, Macrae & Mitchell 2008; Mahajan et al. 2011).

Oxytocin, a neuropeptide involved in social cognition and behaviour in mammals, is involved in increasing relatedness. It reduces social stress, reduces amygdala activation, improves the processing of social and emotional information and increases attachment and empathy toward others (Domes et al. 2007; Hurlemann et al. 2010; Meyer-Lindenberg et al. 2011). Oxytocin might also be involved in negative emotions such as anger and jealousy (Kemp & Guastella 2011), and it not only promotes ‘in-group’ trust and cooperation but also increases aggression toward ‘out-groups’ (De Dreu et al. 2010).

The concept of relatedness links closely to trust (Adolphs 2003; King-Casas 2005). The more individuals trust one another, the stronger the collaboration and the more information is shared. However, high-status individuals tend to trust others more in initial encounters than those of lower status (Lount & Pettit 2012). The degree to which people feel a sense of connectedness and similarity to those around them is directly related to whether or not people feel they are engaging in safe or threatening social interactions (Rock 2008). The phenomena known as ‘in-group preference’ and ‘out-group bias’ refers to the consistent finding that individuals feel greater trust and empathy towards people who are similar to themselves and are part of their same social circles, and greater distrust and reduced empathy towards those who they perceive as dissimilar and members of other social groups. Importantly, increasing intergroup contact can reduce the prejudice observed towards ‘out-group’ members (Dhont et al. 2012) and small groups are less threatening to individuals than larger groups (Rock 2008).

Relatedness is connected to status and certainty. Respect and admiration from peers is much more predictive of a person’s wellbeing than socioeconomic status (Anderson et al. 2012), and those who have difficulty relating to others perceive themselves to be of low social status (Weisman et al. 2011). Further, uncertainty can undermine relatedness (Rock & Cox 2012). Relating to and understanding others usually involves some degree
of uncertainty or ambiguity because the individual has to guess or deduce what other people are thinking or feeling. Therefore, if this is the case, increasing contact between in-groups and out-groups and promoting regular and open communication might be effective in reducing prejudices, especially for those of us who have a high need for certainty.

8.5.5 Fairness

*Just and non-biased exchange between people (e.g. praise for or acknowledgement of one’s efforts, equivalent pay for equivalent work, sharing a candy bar with everyone)*

The concept of fairness relates to our perception of fair exchanges with others (Rock 2008) and that we are treated equally. Fair exchanges are intrinsically rewarding, independent of other factors, whereas unfair exchanges generate a strong threat response (Rilling & Sanfey 2011; Tabibnia & Lieberman 2007; Tabibnia, Satpute & Lieberman 2008). Emotions are integral to judging fairness (Barsky, Kaplan & Beal 2011). When individuals refuse to share or behave unfairly in a way that is not in the best interests of the group, this elicits intense emotions such as disgust and aggression (Gospic et al. 2011). The perception of unfairness in the workplace creates an environment in which trust and collaboration cannot flourish and can negatively affect the physical and mental health of individuals (Robbins, Ford & Tetrick 2012). By contrast, increasing the perception of fairness and reducing unfairness promotes satisfaction and wellbeing, especially in social situations in which sensitivity to interpersonal equality and inequality is heightened.

The following section summarises the neuroscience literature through SCARF® and reflects on the attributes and enablers of an effective workplace culture and the synergy between the models.

8.6 SCARF®ing the Workplace: A Way Forward?

This final chapter provides the answer to my question ‘what drives human behaviour?’ Our emotions drive our behaviour. The brain experiences the workplace primarily as a social system (Rock & Schwartz 2006), and working creatively with the realities of
human nature and meeting fundamental needs has the potential to improve the way we relate to each other. Rock has suggested the five domains of the SCARF® model—status, certainty, autonomy, relatedness and fairness—affect whether individuals feel threatened or rewarded in social settings and, therefore, the degree to which they are able to collaborate effectively (Rock 2008; Rock & Cox 2012). The model demonstrates that threats and rewards provoke such strong responses in individuals and that understanding how to use a person-centred approach to minimise SCARF® threats and increase rewards has the potential to meet fundamental human needs, thus improving wellbeing and the way in which people relate to each other.

Given what this chapter has revealed about human nature, how do we work with this? How can we integrate the SCARF® principles into the workplace? Rock and Tang (2009) outlined how the SCARF® domains may be the factors that underpin workplace engagement. The authors suggest that existing models that assess workplace engagement measure various domains of SCARF® but with uneven weighting and without including all domains. Rock et al. (2010) postulated that the SCARF® model explains in part why change is so difficult and how it could be used to offset the threats associated with the change process. Other work within the field of neuroleadership has suggested that it might be possible for individuals to use SCARF® as a cognitive tool to predict an emotional event or threat (Lieberman 2009), regulate an existing threat (Gross 2003; Ochsner 2008) and, after an emotional event, to help explain and understand the situation (Rock & Cox 2012). This increased awareness of emotion in social interaction may reduce uncertainty and conflict over time.

The SCARF®-SA (Self-Assessment) tool illustrates the order in which the SCARF® elements matter to an individual (Results Coaching Systems 2010). If everyone in the workplace undertook this assessment and knew which of the five domains were key drivers for them (and for others), it might help them to understand why individuals react so strongly in certain situations while others do not. It could also help to explain the reactions of others around them. This might be one way to raise awareness of the importance of our behaviour within the workplace. Of interest, neuroscience also points to an alternative strategy called mindfulness that encourages individuals to pay attention to how their own mind works. Mindfulness raises an individual’s awareness of present
thoughts, emotions or actions (Tang & Posner 2008), focuses attention (Brefczynski-Lewis et al. 2007; Tang et al. 2007), has a positive effect on wellbeing (Shapiro et al. 2008), enables self regulation of emotion (Beauregard, Levesque & Bourgouin 2001; Botvinick et al. 2001) and therefore might improve the way individuals relate to each other.

The work of contemporary neuroscience and neuroleadership resonate with the work of Manley et al. (2011) because the SCARF® domains mirror many of the characteristics proposed as being crucial to the development of an effective workplace culture (Chapter 7). The neuroscience literature suggests that to achieve an effective workplace we need to ensure the attributes and enablers pay due regard to fundamental human needs. This is key to explaining why person-centred cultures work; they work, at least in part, because threats within the five social domains captured within the SCARF® framework are minimised and because rewards are maximised. That is, workplaces with the enablers and characteristics of effective workplaces foster a sense that everyone is working together, goals and values are shared, individuals support each other, there is freedom to discuss openly what is working and what is not and processes are in place to aid decision making and ensure the system is fair (Manley et al. 2011).

Leaders and managers could increase workplace engagement by focusing energies on creating an effective workplace culture utilising the SCARF® principles (Rock 2008; Rock & Cox 2012). This would involve helping people to feel good about themselves, letting them know they are valued, being inclusive, communicating expectations clearly and sharing information, enabling others to make decisions and acknowledging contributions, offering choice, providing opportunities for learning and development and supporting efforts to build good relationships and collaborative teams. Such behaviour could prompt reward responses, increase emotion regulation and working memory capacity, improve cognitive thinking and increase productivity. In such a workplace culture, the team would ‘own’ best practice and continue to explore what that means in the local context through everyday practice and evaluation of any new evidence that occurs. Transformational practice development (tPD), with its focus on person-centred cultures that uses processes of collaboration, inclusion and participation (Manley, Solman & Jackson 2013, p. 146) then, has the potential to provide an
approach to reduce the identified SCARF threats. Manley et al. (2013, p. 8) define an effective workplace culture as:

A local workplace characterised by the experience of three value sets by all who come into contact with it: a focus on person-centredness, collaborative, inclusive and participative ways of working; and a focus on providing effective care. These values are embedded in local formal systems of evaluation, learning, development and stakeholder participation that reflect and sustain them. Effective workplace cultures are recognised by flourishing of all involved, consistent achievement of standards and goals, evidence-based and continuous development, improvement and innovation in practice linked to the needs of patients, and, empowered and committed staff. These cultures are enabled by transformational leaders, skilled facilitation and role clarity and are complemented by organisational readiness with a flattened and transparent management structure and supportive human resource department.

The links between this approach to leadership and the ways of working associated with the SCARF model and tPD as an intervention to transform individuals, practice and cultures are obvious. Exploring further these potentially causal links, and the implications for evolving a relatively ‘hard science’ to support facilitated tPD approaches to enhancing workplaces and engaging staff more positively would enrich arguments for its use; particularly given the length of time and other intricacies associated with evolving robust evidence of its use as a complex intervention (Manley, Crisp & Moss 2011). Just as importantly, however, understanding the neuroscience mechanisms involved in tPD work, and working with these in the day-to-day implementation of transformational processes (whether these be named as tPD or otherwise) has the potential to assist in the development of transformational leaders and facilitators with the expertise required to support complex processes (see Crisp and Wilson (2011)).

A shift in thinking within health care is required to create a culture in which values and ways of working collaboratively are discussed, critical conversation occurs without threat, local teams work with their own data to explore and improve their practice, and individuals find better ways of having their needs met. Services would need to be flexible, existing hierarchical and restrictive processes altered, and creativity and innovation nurtured. This process has begun in NSW through the Essentials of Care (EoC) Program, a continuous quality improvement project that works with teams in the
practice environment to improve workplace culture (Nursing and Midwifery Office 2013). Anecdotal evidence suggests emerging work shows promise, but the work from the EoC program is unpublished at this time. Further, the relationships between practice development concepts and process outcomes have not as yet been clearly explicated within an impact framework (Manley, Crisp & Moss 2011).

No existing publications link neuroscience and neuroleadership to transformational practice development; however, it appears they share similar elements and aims. Contemporary neuroscience gives us clues to what we need to understand about the realities of trying to do complex things within complex environments and the social processes that enable or hinder that. Surely, this insight into the drivers of human behaviour can only enhance an approach that is primarily person centred.

8.7 Summary

The confluence of technological advances, increasing patient acuity, finite resources and increasing demand for high performance and quality care from administrators and consumers means assessing the effect of our interventions is now a health care priority. The work of this thesis has described the knowledge generated and learning achieved as I aimed to establish robust evidence and reduce inconsistencies in incubator humidity use in the management of extremely preterm infants. My doctoral journey began with the development of a thesis plan for the design and conduct of an RCT to identify optimal levels and duration of humidity and the effects of humidification on clinically important health outcomes. However, circumstances and challenges shaped my journey and I ventured down a very different and enlightening path. My experiences of the NICU environment together with the literature and data collected from the survey presented in Chapters 3 through 6 highlight the challenges of knowledge generation and utilisation and the complexities of the practice environment.

The work found that it is the individual characters and how they relate to each other that determine the culture within the workplace and how care is provided. My increasing awareness of the complexities and messiness of the social world of the practice environment motivated me to gain an understanding of the elements that comprise the
clinical context and how context influences workplace culture. The work of this thesis identifies the attributes and enablers of an effective workplace culture (Manley et al. 2011) and how implicitly embedded within this is a way of people working together that improves life for both clinicians and patients. The thesis also makes explicit the drivers of human behaviour (neuroscience) that explain why the workplace cultures proposed are effective and why threats to SCARF® (status, certainty, autonomy, relatedness and fairness) are less likely to be triggered (neuroleadership). Further, neuroscience takes this a step further and encourages individuals to pay attention to how their own mind works (mindfulness)—an intervention that might also improve the way individuals relate to each other. Finally, the thesis suggests using an approach that makes each of these elements explicit and has the potential to enable clinicians to develop healthy relationships, and to improve their practice environment and the care they provide (tPD).

Without support of and investment in clinicians, transferring evidence into positive patient outcomes will continue to remain elusive; we need to meet the needs of clinicians before they can meet the needs of patients in complex environments. This work makes clear that the challenges within the workplace in which clinicians are embedded need to be discussed and solutions sought, and that effective workplace cultures need to underpin health care policy and academic curricula. Further, future research needs to pay due attention to the individual characters and their interaction with each other and with contextual factors within the workplace. We owe it to our patients to act, to take up this challenge because ‘without action the rhetoric will remain rhetoric’ (Manley et al. 2011, p. 20).

8.9 Conclusion

This journey began with my search for certainty, so it seems appropriate that this is where it ends. I sought clear evidence to optimise incubator humidity use in the NICU to reduce uncertainty and inconsistencies in practice. However, certainty proved to be elusive; instead, I found uncertainty, in many guises: in clinical practice, in the generation and utilisation of knowledge, in patient outcomes and in relationships within the workplace. Scott et al. (2008) stated that certainty must be present to create and
sustain clinical environments that are ideal for research utilisation. It is unlikely that we can ensure absolute certainty in decision making and practice within intensive care environments. However, the work of this thesis suggests that it might be possible to create a workplace culture in which individuals are valued and the system seems fair so that uncertainty has less of an effect.
Appendix 1

Incubator Humidity for Preterm Infants:
Telephone Questionnaire re Current Practices

1. In your unit, do you provide incubator humidity for preterm infants?
2. Do you have a unit policy on the provision of incubator humidity for preterm infants?
   ? can I have a copy
3. What type of incubator is used for this purpose?
4. At what gestational age or birthweight is humidity commenced?
5. How soon after birth is incubator humidity commenced?
6. Initially what percentage of humidity do you use?
7. Is the percentage of humidity used dependent on gestational age or birthweight?
   If so please state.
8. What are the lowest and highest levels of humidity used within your Unit?
9. What is the duration of humidity administration?
10. Does this vary depending on gestational age or birthweight?
11. Can you briefly describe your weaning policy?
12. What do you perceive to be the benefits of incubator humidity?
13. Have you encountered any problems with incubator humidity use?
14. Any other comments about humidity use?
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