Appendix 3 (as supplied by the authors): Study protocol for Evidence-based Practice for Improving Quality (EPIQ)

SUMMARY OF RESEARCH PROPOSAL

A major weakness in our health research enterprise is the inability to effectively, efficiently and rapidly translate knowledge into improved quality of care, better patient outcomes and reduced costs. Preterm birth is the most important cause of perinatal mortality and long-term neurodevelopmental morbidity. It complicates 76 of every 1000 births in Canada, and its incidence has risen over 30% during the past 2 decades. The costs of preterm birth are estimated to exceed $1 billion annually in Canada and include NICU care, which is expensive and often prolonged. Current research efforts to address preterm birth are aimed at prevention or at improving outcomes. Unfortunately, little is known about how to reduce preterm births and outcomes of preterm infants have improved little in recent years.

This research program is designed to improve outcomes and reduce costs through a better understanding of how different practices and risks affect long-term outcomes of preterm infants, and how improved methods of knowledge translation can enhance quality of care. The proposal contains 5 projects integrated by the PARIHS framework. The PARIHS model is a guide for implementing evidence-based practice change and is based on three components: **Evidence, Context** and **Facilitation**. Maximizing the quality of these variables will ensure successful implementation of practice change.

To carry out this program of research, we will establish a national neonatal follow-up database using standardized assessments of all infants born at less than 29 weeks gestation. Then, the follow-up database will be linked to existing databases that collect standardized information on sociodemographic factors, outcomes, practice and resource use data for all high risk pregnancies, infants admitted to any tertiary NICU in Canada, selected NICU infants needing surgery, and infant pain evaluation and management to form a single, novel, integrated Maternal-Infant Care (MICare) Database.

Project 1 will generate high quality **Evidence** by meeting two objectives. First, the MICare Database will be used to study how biological, sociodemographic, environmental and treatment risks during pregnancy, childbirth and infancy interact to affect short and long-term infant outcomes. Then, variations in outcomes will be used to identify practices associated with good or poor long-term neurodevelopmental outcomes, for design of potential practice change interventions to improve quality of care.

Project 2 will augment the quality of the **Context** or the environment in which healthcare services are provided. In this project, we will establish a research-focused virtual research community that will allow investigators and clinicians to collaborate and share findings online. Selective access will also be provided to NICU staff. Later, customized decision-support tools will be developed based on outcomes of Project 3. Also, evaluation of access to the virtual research community and decision-support tools will be used as a measure of the extent to which knowledge transfer is taking place.

Project 3 develops an advanced Version II of the Evidence-based Practice identification and Change (EPIC) system to more efficiently **Facilitate** implementation of practice change. EPIC-II is based on 3 features: (a) systematic review of evidence in the published literature, (b) quantitative and qualitative analysis of outcomes and practices to identify practices associated with good or poor outcomes for targeted change, and (c) use of a collaborative network of clinicians, researchers and administrators. Evidence from Project 1 and the decision support system from Project 2 will be used to augment this project.

Projects 4 and 5 will provide further **Evidence** to understand factors that affect the quality of infant care and contribute directly to Projects 2 and 3. Project 4 will use the best practices identified by Projects 1 and 3 to develop and validate indicators of quality of care that can not only monitor outcomes but also guide continuous quality improvement efforts. This information will be added to the decision support tools in Project 2. In Project 5, prognostic tools will be developed for preterm birth outcomes to provide updated

Appendix to: Lee SK, Shah PS, Singhal N, et al.; Canadian EPIQ Study Group. Association of a quality improvement program with neonatal outcomes in extremely preterm infants: a prospective cohort study. *CMAJ* 2014. DOI:10.1503/cmaj.140399.

information for family counseling and decision making. This information will also be added to the decision support tools developed in Project 3.

This program also includes a significant training component that will leverage 3 existing CIHR-funded Strategic Training Initiatives in Health Research (STIHR) to provide tremendous opportunities for training a new generation of health researchers in knowledge translation and healthcare improvement.

Appendix to: Lee SK, Shah PS, Singhal N, et al.; Canadian EPIQ Study Group. Association of a quality improvement program with neonatal outcomes in extremely preterm infants: a prospective cohort study. *CMAJ* 2014. DOI:10.1503/cmaj.140399.

SUMMARY OF PROGRESS

During the past ten years, our team of researchers has laid important groundwork that now make it feasible for us to achieve the objectives of this proposal.

1. Progress towards establishing an integrated national maternal-infant database

In 1995, Shoo Lee founded the Canadian Neonatal Network (CNN) that includes all 30 neonatal intensive care units (NICU) across Canada. He established a standardized national research database that collects sociodemographic, outcomes, practice and resource use data from all infants admitted to a tertiary NICU in Canada. Since then, CNN has received 10 peer-reviewed grants, published over 100 peer-reviewed articles, and was awarded the Knowledge Translation Award by CIHR in 2004.

In 2002, Shoo Lee, together with 7 other members of this proposal, founded the Neonatal-Perinatal Interdisciplinary Capacity Enhancement (NICE) Team with CIHR funding (2002-2008). This supported the formation of the Canadian Pediatric Surgery Network (CAPSNet, led by Erik Skarsgard) in 2004 and the Canadian Perinatal Network (CPN, led by Robert Liston and Laura Magee) in 2006. Operating grants were obtained from CIHR by CAPSNet (2004-2009) and CPN (2006-2009) to establish national databases to study complex congenital anomalies and pregnant women admitted to hospital with preterm labor at <29 weeks gestation. The Canadian Association of Pediatric Surgeons and BC Children's Hospital Foundation have provided additional funds to extend the CAPSNet and CPN databases respectively to 2010. Both databases share common definitions, protocols and linkable database systems with CNN. In 2006, Bonnie Stevens formed the Canadian Pediatric Pain Research Network (CPPRN) and obtained CIHR funding (2006-2011) to establish a database to study pain in children. Although these databases provide information on short-term outcomes, there is lack of standardized long-term neurodevelopmental outcomes, which is vitally important for neonatal-perinatal research.

An exciting and unique opportunity exists to establish a standardized national neonatal follow-up database and link with the CPN, CNN, CAPSNet and CPPRN databases to create the world's first population database of very preterm infants that links the entire period from pregnancy to infant follow-up for research. This Maternal-Infant Care (MICare) database will open tremendous opportunities for study of risks across the entire period, and how they interact to affect long-term outcomes. This will provide insights into how to design interventions to improve care and outcomes for very preterm infants. We propose to seize the opportunity to establish this database as a world class resource for research in this proposal.

2. Knowledge Management & Decision Support Tools

In 1998, Robert Hayward established the Center for Health Evidence at the University of Alberta and developed the VIVIDESK^{TM} technology as a computerized knowledge management and decision support system for clinicians. Since then, he has adapted the technology to support several environments, including cardiac care and children's care, and demonstrated the utility of a virtual research community for knowledge management and transfer. The technology is now ripe for adaptation in order to examine the context within which clinical decisions are made, and to provide computerized decision support tools to facilitate knowledge translation in neonatal-perinatal care. We propose to adapt this technology to provide a virtual research community and decision support for neonatal-perinatal care.

3. Models for Knowledge Translation to Improve Quality of Care

Since 1996, CNN researchers have conducted a program of research aimed at examining variations in outcomes and developing new models for effective knowledge translation to improve quality of care. In 2001, Shoo Lee et al[28] patented the SNAP-II instrument for benchmarking NICU outcomes. In 2001, Synnes et al[6] demonstrated that outcome variations were associated with practice differences. In 2004, MacNab et al[54] used multilevel modeling methods to quantitate the attributable risks associated with adverse NICU outcomes. Building on these developments, in 2004, Shoo Lee[86] developed the Evidence-based Practice Identification and Change (EPIC) model for knowledge translation to improve quality of care and conducted a cluster randomized controlled trial of 12 NICUs that demonstrated 40% reduction in infection rates and 20% reduction in bronchopulmonary dysplasia rates. We now propose to further develop the EPIC model to target multiple outcomes simultaneously to reduce the time and costs for implementing quality improvement measures.

A. TEAM RESEARCH PROGRAM

OVERVIEW

Our CIHR Team in Maternal-Infant Care (MICare) will address the important health care issue of knowledge translation to improve care for preterm infants by conducting 5 projects that link evidence with context and facilitation. We will create a novel national population-based database that links the entire period from pregnancy to childbirth to infancy for research. The 5 innovative projects will use this database to generate new knowledge about the risk determinants of preterm birth, create new models for knowledge translation and quality of care improvement, develop new measurement and monitoring systems, and provide better tools for family counseling and decision making. We will leverage strengths from across Canada by including 18 carefully selected clinical, health services and population health researchers from 7 universities, and building upon four well established national neonatal-perinatal research networks involving 30 hospitals across Canada. We will actively facilitate training of new leaders in research and leverage 3 CIHR funded STIRH training programs. Our team will add value and provide a novel database platform that will generate new knowledge for improving care for pregnant women and their infants. Over the next 5 years, our team will transform the face of preterm pregnancy and infant care in Canada and internationally.

A.1 The Health Problem

A major weakness in our health research enterprise is the inability to effectively, efficiently and rapidly translate knowledge into improved quality of care, better patient outcomes and reduced health care costs. For instance, 25 years after Liggins et al[1] and others[2,3] first reported that antenatal corticosteroid treatment of women expected to give birth preterm significantly reduced the incidence of respiratory distress syndrome and mortality among newborn infants, Chien et al[4] found only 59% of eligible preterm infants admitted to Canadian neonatal intensive care units (NICUs) received antenatal corticosteroid treatment. Furthermore, it was estimated that increased use of antenatal corticosteroid treatment for preterm births could reduce neonatal mortality in Canada by 10%. Lee et al[5] found significant variation in outcomes among Canadian NICUs and others have reported that variations in outcomes may be attributable to differences in practice.[6,7,8,9] These studies demonstrate current mechanisms for knowledge translation are slow, uneven and ineffective. More importantly, improved translation of knowledge into practices and policies could potentially improve patient outcomes and reduce costs of health care.

Preterm birth is a prime area for developing knowledge translation models to improve quality of care. Preterm birth is the most important cause of perinatal mortality and long-term neurodevelopmental morbidity, including: cerebral palsy, deafness, blindness, learning disability and behavioral disorder.[10,11,12,13,14] Seventy-six of every 1000 births in Canada are complicated by preterm birth and its incidence has risen over 30% during the past 2 decades[10]. The Canadian Perinatal Surveillance System (CPSS, 2004) reported the preterm birth rate as 8.3% in the year 2004, and in 1994 it was only 6.8%.[15] The costs of preterm birth are estimated to exceed $1 billion annually in Canada and include NICU care, which is expensive, often prolonged, and accounts for 10% of all health care costs for children.[16] Improving outcomes for preterm infants has the potential to decrease health care costs and to enhance outcomes for all pregnant women and their infants. Current research on preterm birth has focused on prevention or outcome improvement. Unfortunately, with the exception perhaps of progesterone, which shows promise of reducing the rate of spontaneous preterm birth,[17,18] little is known about how to reduce preterm births and outcomes of preterm infants have shown little improvement in recent years.[16,19] This proposal is designed to improve outcomes of preterm births and reduce costs through a process that will utilize the PARIHS framework to generate the **Evidence**, provide the **Context** and **Facilitate** the translation of knowledge into practice change.

A.2 Objectives

1. *Establish a multi-disciplinary team* to conduct innovative inter-disciplinary research that facilitates knowledge translation by building upon existing national neonatal, perinatal, surgical and pain research networks
2. *Create a novel, integrated national database* that will link information for the entire period from pregnancy to childbirth, neonatal care and developmental follow-up, to facilitate examination of how the risk factors throughout this period interact to affect outcomes

3. *Conduct 5 innovative projects* that will help us to better understand the evidence, and contextual and organizational factors influencing practice change, develop and test new models for quality improvement, and transform the way we translate knowledge to improve quality of care
4. *Build partnerships between researchers, clinicians, decision makers and community partners* to provide an on-going system for research that will improve our ability to translate evidence into improved care and outcomes for pregnant women, infants and their families.

A.3 Hypotheses

We hypothesize that high quality evidence, introduced into a highly supportive clinical environment will produce the desired changes in professional and patient outcomes. As a result, at the interface of these elements, where the integration of these projects can be recognized, knowledge translation outcomes will be optimized. Specific hypotheses for each of the 5 projects in this proposal are given in the project descriptions in Sections A.10 to A.15.

A.4 Approach - using the PARIHS Conceptual Model

We will conduct five projects, which will be integrated using the Promoting Action on Research Implementation in Health Services (PARIHS) framework. The PARIHS framework[20,21] incorporates **evidence**, **context** and **facilitation;** 3 elements considered essential for successful translation of research into practice. This integration accounts for the complexity of implementing practice changes and each is rated on a continuum from low to high[16].

Evidence includes research evidence, clinical expertise and local data/information[16]. Research evidence that is rigorous, relevant, valued and "generalizable" is highly rated on the evidence to practice continuum.[21,22,23] The value of high quality evidence is rooted in Evidence-Based Medicine, where its application from systematic reviews into clinical practice is thought to produce high quality patient care.[24] Evidence from clinical expertise is high when the experience is reflected on, tested, valued and relevant.[22] Local evidence, from audit and performance data,[21,22,23] is high when data are valued, rigorously evaluated and interpreted[22]. These 3 forms of evidence are integrated in the Evidence-based Practice Identification and Change (EPIC) intervention in Project 3.

Context is the environment or setting where evidence-based practice changes occur[22,,25] and includes organizational culture, leadership and evaluation.[22] Culture refers to "a way of thinking about or viewing an organization, comprised of basic assumptions, values, artifacts and creations"[25] Culture is considered high when there is regard for individuals, a supportive learning environment, available resources, and alignment of the change initiative with the organization's strategic goals.[22] Effective leadership involves leaders who assume a decentralized role where they influence, enable and empower others to share a common vision through role clarity, effective teamwork and decision making.[25] Evaluation of the KT strategies is enhanced when multiple sources of information are integrated. Performance audits and feedback about the intervention will enhance receptivity to implementing pain practice changes[25].

Facilitation is the enabling of evidence into practice, which takes the quality of the evidence and specific unit/context into consideration.[22,23,26] As knowledge translation and utilization are social processes[20], evidence requires tailoring to the needs of environment or setting before it will be acceptable to clinicians[21]. Effective facilitators provide face-to-face communication and focus on enabling individuals to change practice.[5]

Conceptual Diagram: Figure 1 is a conceptual diagram showing the PARIHS framework, and how the 5 projects integrate together within the framework.

A.5 Research plan

This is a 6 year research proposal consisting of a core database facility and 5 projects, which will be conducted at all 30 hospitals across Canada that provide tertiary perinatal, NICU and surgical care, and neonatal follow-up screening (Appendix C). Together, these projects lay important foundations for improving care of preterm infants. Funding is only sought for 5 years because the first year of data collection will be funded by 2 on-going CIHR grants.

Core Facility: We will begin by creating a national Canadian Neonatal Follow-Up Network (CNFUN) database of all infants who are born at less than 29 weeks gestation in Canada from July 1, 2007 to June 30,

2010 (Year 0 to Year 2, some data collected retroactively), using standardized assessments at 18 and 36 months of age (Year 2 to Year 5). We will link the new CNFUN database with the databases of 4 existing national networks (Canadian Neonatal Network [CNN], Canadian Perinatal Network [CPN], Canadian Pediatric Surgery Network [CAPSNet], Canadian Pediatric Pain Research Network [CPPRN]) to form the Canadian Maternal-Infant Care (MICare) Database. This database will bring together research, clinical experience, patient experience and local information to provide high quality evidence about how risk factors interact to affect outcomes.

Project 1 will utilize the MICare Database from Year 0 to examine the **Evidence** related to how patient risks and therapeutic factors during pregnancy, childbirth and infancy interact and affect long-term infant developmental outcomes. It will also examine variations in outcomes and how these are linked to practices. The results will provide insight into how practice change interventions can be designed to improve long-term outcomes for preterm infants in Project 3.

Project 2 will provide high quality **Context** for the proposal by establishing a virtual research community (VRC) to link team members and NICU staff (Year 1), developing and deploying customized decision-support (CDS) tools for clinicians and administrative leaders (Years 2-3), and evaluating usage of the VRC and CDSs (Years 2-5). The VRC will be used to **Facilitate** implementation of practice changes in Project 3.

Project 3 will use the EPIC method developed by Lee et al[27] to **Facilitate** the implementation of evidence into practice (high quality facilitation). Since EPIC only targets single outcomes, we will develop and evaluate a next generation EPIC-II model that will target multiple outcomes simultaneously and develop comprehensive best practice strategies for NICU care of preterm infants. Baseline data collection and systematic literature reviews will be conducted in Year 0, followed by outcome improvement interventions in Years 1-3. Intervention information will be fed back to the team members working on Project 2 for inclusion in the CDS system. Data analyses and interpretation of long-term neonatal follow-up outcomes will be performed in Years 4-5.

Project 4 will identify and validate indicators of quality of care that will not only monitor outcomes but also guide continuous quality improvement efforts (high quality **evidence, context** and **facilitation***)*. Year 4 will be used to systematically review the scientific literature and develop potential indicators. The indicators will be authenticated and validated against the MICare Database in Year 5.

Project 5 will generate an actuarial assessment of newborn outcomes that can be used for prognostication (high quality **evidence** and **facilitation**). In Year 2, short-term neonatal outcomes will be assessed using the MICare Database. In Year 3, a scoring system for short-term outcomes will be established and analyses will begin on long-term outcomes. Analyses will be completed in Years 4-5 and the scoring system will be disseminated to Canadian NICUs.

A.6 Milestones

Milestones were developed for each project based on the project's timeline, goals and activities. Milestones reflect the integrated nature of projects and the segments of each project that can be completed independently from all other projects. A summary of the milestones is found in Figure 2.

A.7 Team Linkages

The MICare Team is multidisciplinary and multi-institutional, with expertise in neonatology, maternal-fetal medicine, nursing, management, epidemiology, statistics, health informatics, economics, quality improvement, organizational change, qualitative research and knowledge translation. The 18 team members are all experienced researchers with established track records of funding, publication and collaborative research, and represent the top talent in neonatal-perinatal clinical, population and health services research from across Canada. Several are members of the Neonatal-Perinatal Interdisciplinary Capacity Enhancement (NICE) Team that was funded by CIHR from 2002-2008 to conduct research projects in collaboration with CPN, CNN and CAPSNet. The NICE Team published over 100 articles and was instrumental in the work that won the Canadian Neonatal Network the Knowledge Translation Award from CIHR in 2004. Thus, the MICare Team builds upon a successful tradition of collaborative research from the NICE Team. In this proposal, MICare Team members will work closely because the projects are

inter-linked and utilize results from other projects. Consequently, team members will consult and share findings frequently. Many team members also participate in more than one project.

The MICare Team will link with an extensive network of clinician-researcher and decision-maker collaborators. Five national research networks (CPN, CNN, CAPSNet, CPPRN, CNFUN) representing clinician researchers and decision makers from 30 hospitals and 16 universities across Canada will participate in this program of research. They will help formulate the research agenda and engage stakeholder participation in projects. They will work closely with the MICare Team to translate evidence and implement practice change strategies, evaluate their impact, and disseminate the results.

The MICare Team has strong linkages with professional bodies (Fetus & Newborn Committee [FNC] of the Canadian Pediatric Society, 8 Provincial Perinatal Organizations [PPO]) that will use our research findings to set practice guidelines. Regulatory agencies (Canadian Association of Pediatric Health Centers [CAPHC], Canadian Perinatal Surveillance System [CPSS] from the Public Health Agency of Canada, regional health authorities) and community partners (Families Resource Program of Canada [FRP]) will help formulate the research agenda and disseminate knowledge widely to stakeholders. CAPHC will also utilize our research findings to implement quality improvement indicators and policy change.

Team members are experienced mentors and many are key mentors of CIHR-funded STIHR training programs. We will leverage funding from 3 existing STIHR programs. MICare trainees will have access to their training programs and link with their trainees and mentors.

A.8 Integration of Results

The 5 projects form an integrated package that brings together the different elements of the PARIHS framework, so that the interplay of **Evidence, Context** and **Facilitation** results in practice change and improved outcomes. The MICare Database provides a core resource for all 5 projects. This linked database is important because it permits analysis of how risk factors during the antenatal, intrapartum and postpartum neonatal periods interact to impact long-term infant outcomes. Project 1 uses this **Evidence** to examine how risk factors interact to impact outcomes, and develops the basis for design of practice interventions that will be used in Project 3. Project 2 examines the **Context** in which clinicians and decision makers utilize evidence, and **Facilitates** use of evidence in clinical care and decision making in Project 3. Project 3 develops a new quality improvement model that uses **Evidence** from Project 1 to identify potential practice change interventions, examines the **Context** of individual and organizational behavior using qualitative methods, **Facilitates** implementation of practice change strategies using decision support systems from Project 2, and evaluates the impact of these changes. Project 4 develops an indicator system that can be used to **Facilitate** establishment of an on-going quality monitoring and improvement system so that the impact of Project 3 can be sustained over the long-term. Project 5 utilizes the evidence from Project 1 to develop prognostic tools that can **Facilitate** family counseling and clinical decision making. Thus, the database, projects and results are well integrated through the PARIHS framework. Projects 1 and 2 combine to bring together different components of **Evidence, Context** and **Facilitation** in a way that enables Project 3 to be effective at implementing practice change, and Projects 4 adds value by creating an on-going quality monitoring and improvement system that will sustain the impact. Project 5 extends the use of **Evidence** to families for counseling and decision making.

A.9 Anticipated value of the results

This program of research will re-define our approach to knowledge translation and quality improvement in all areas of health care, and significantly change how perinatal-neonatal care is delivered in Canada and elsewhere. The MICare Team will demonstrate how multidisciplinary researchers, clinicians, decision makers and community groups can collaborate in a practical way to effectively translate knowledge into practice and policy change to improve quality of care. We will demonstrate the value of a linked population database (MICare Database) that spans the entire period from pregnancy to childbirth, infancy and developmental follow-up. We will address important deficiencies in the follow-up literature, and demonstrate how baseline risks and treatment factors interact during pregnancy, childbirth and infancy to affect long-term developmental outcomes, and how these factors can provide insights into how to improve quality of care. We will develop new desktop support tools and demonstrate how they can facilitate decision

making by clinicians and decision makers. We will demonstrate how a unique scientific process for comprehensive quality of care improvement (EPIC) can improve outcomes and reduce the time and costs for quality improvement. We will develop a system of indicators that can both monitor outcomes and provide a mechanism for evaluating quality and sustaining improvement. We will show how a new prognostic tool can facilitate family counseling and decision making in sick infants. We will also provide a tremendous training opportunity for new researchers, and groom them in a multi-disciplinary environment. In summary, our research will yield a comprehensive, evidence-based programmatic approach to knowledge translation that improves outcomes in a multi-dimensional way, and can sustain the improvements over time.

A.10 Core Facility: Create an integrated Maternal-Infant Care (MICare) Database

We propose to establish a new standardized neonatal follow-up (CNFUN) database and link it with the CNN, CPN, CAPSNet and CPPRN databases (described below) to form an integrated Maternal-Infant Care (MICare) Database. This database will be a key resource for this program of research.

A.10.1 Project leader and participants

Shoo Lee & Nicola Shaw (MICare Leads), Reginald Sauvé & Saroj Saigal (CNFUN Leads), Robert Liston, Laura Magee, Erik Skarsgard, Bonnie Stevens. Participating networks include:

(a) *Canadian Neonatal Network (CNN):* CNN was founded in 1995 by Dr Shoo Lee and includes all 30 tertiary NICUs across Canada. Since 1996, CNN has maintained a national standardized database[528] (funded by participating hospitals) of sociodemographic, outcomes, practice and resource use data on all infants admitted to any tertiary NICU across Canada. Health care professionals, health services researchers and health administrators actively contribute to clinical, epidemiological, health services, health policy and informatics research studies aimed at improving efficacy and efficiency of neonatal care.[29] CNN has published over 100 peer-reviewed articles and was awarded the Knowledge Translation Award by CIHR in 2004.

(b) Canadian Perinatal Network (CPN): CPN was founded in 2005 by Drs Robert Liston and Laura Magee, and includes all 22 tertiary Canadian perinatal units. CPN is funded by CIHR and BCCH Foundation (until August 2010) to establish a standardized national database of all pregnant women <29 weeks gestation who are at risk of preterm birth and admitted to a tertiary hospital, and to (i) examine variations in outcomes and practices, for the major causes of spontaneous and indicated very preterm birth; (ii) identify obstetric practices that are associated with favorable and unfavorable outcomes for further intervention studies; and (iii) study variations in resource use associated with obstetric practice and tertiary perinatal characteristics.

(c) Canadian Pediatric Surgery Network (CAPSNet): CAPSNet was founded in 2004 by Dr Erik Skarsgard and includes all 16 Canadian pediatric surgical units. CAPSNet is funded by CIHR and CAPS (until October 2010) to establish a standardized national database to study risks, outcomes and practices associated with complex anomalies, beginning initially with gastroschisis and congenital diaphragmatic hernia.

(*d) Canadian Pediatric Pain Research Network (CPPRN):* CPPRN was established by Dr Bonnie Stevens in 2006, with CIHR funding until 2011. CPPRN collects sociodemographic data, type and frequency of painful procedures and pain assessments, pharmacologic and non-pharmacologic (e.g. physical and psychological) interventions and information on the research unit where the patient was treated.

(e) Canadian Neonatal Follow-Up Network (CNFUN): We will establishment a national database using standardized neurodevelopmental assessments at 18 months corrected and 36 months chronologic age, for all infants born in Canada at less than 29 weeks gestation. This will permit examination of risk factors affecting long-term outcomes. CNFUN and its database will be led by Drs Reginald Sauvé and Saroj Saigal.

A.10.2 Objectives

- To create a national neonatal follow-up database (CNFUN Database) using standardized assessments of all infants who are born at less than 29 weeks gestation, fitting with existing programs as closely as

possible and using standardized neurodevelopmental assessment approaches at 18 months corrected age and 36 months chronologic age (Sauvé & Saigal – CNFUN Leads)

- Link the new CNFUN database with the CPN, CNN, CAPSNet and CPPRN databases to create a single integrated national Canadian Maternal-Infant Care (MICare) Database (Lee – MICare Lead)

A.10.3 Approaches

For the first time in the world, this database will link population-based sociodemographic, clinical practice, outcomes and resource use data for high risk pregnancies and infants throughout the entire period from pregnancy to childbirth, infancy and developmental follow-up. This unique database will enable us to study how the interactions between determinants, mechanisms and processes of care affect pregnancy and infant outcomes over both the short and long-term.[30] This knowledge is invaluable for designing interventions to improve care for preterm pregnancies and infants.

A.10.4 Research Plan

(a) CNFUN Database: We will enroll all infants (n=3600) born at less than 29 weeks gestation and admitted to a NICU from July 1, 2007 to June 30, 2010. Informed consent will be obtained. An interview and standardized assessments will be performed at all 22 follow-up clinics at 18 months corrected and 36 months chronologic age. Attendance of eligible infants at follow-up clinics exceeds 85% in Canada.
(b) MICare Database: The CNFUN database will be linked with data from CPN, CNN, CAPSNET and CPPRN databases to create an integrated database.

A.10.5 Methods

(a) CNFUN Database Variables:

The assessment tools to be used at 18 months adjusted age will be introduced at 22 existing neonatal follow-up clinics. Sociodemographic and post discharge health utilization data (Appendix D), growth (weight, length and head circumference), physical examination and neurodevelopmental assessments will be collected to help determine the presence of severe and minor disabilities and their functional consequences. Two formal assessment tools will also be used: Bayley Scales of Infant and Toddler Development III (BSID)[31] and the Gross Motor Classification System for cerebral palsy (GMCS).[32] The BSID tests cognitive, fine and gross motor function, language, adaptive behavior and social-emotional impairments. It is the most commonly used standardized assessment tool employed in Neonatal Follow-up programs, it has good discriminative validity, correlates with other assessment tools and is reliable. Examiners at each site will be trained to ensure reliability. The GMCS is a simple, validated method with good inter-rater reliability for diagnosis of cerebral palsy related disability (Appendix E). The findings of the 18 months assessment will be used to categorize the infants according to major disability, minor disability and no disability.

A questionnaire level assessment is currently planned for 36 months; one of the major reasons for this is validation of the findings at 18 months. The assessment tools to be used at 36 months chronologic age are to be administered by mailed questionnaire and telephone interview. The interview will confirm sociodemographic measures, further post discharge health utilization data and parental concerns regarding neurodevelopmental outcomes. Three formal assessment questionnaires will also be used: Health Status Classification Pre-School (HSCS-PS), Ages and Stages Questionnaire (ASQ) and Behavior Rating Inventory of Executive Function (BRIEF-P). The HSCS-PS is a validated, simple to use, multiattribute system that measures 12 health status attributes (vision, hearing, speech, emotion, dexterity, self-care, cognition, pain, general health and behavior) (Appendix F). ASQ correlates well with more formal tests of development and intelligence and has many advantages, including: ease of administration, low cost, and completion by parents in just 10-15 minutes. Results are dichotomous for five domains (communication, gross motor, fine motor, problem solving and personal-social). Extensive validity and reliability testing with other developmental and intelligence tests have been performed. At 36 months the sensitivity was 90% and specificity 92% with an overall agreement of 86%. (Appendix G). The final tool, the BRIEF-P, comprises 63 items to provide index scores of inhibitory self-control, flexibility and emergent "metacognition". The structure of this scale has been validated and it has good reliability and validity. It is the best tool at this age for evaluation of executive dysfunction (Appendix H).

(b) CNFUN & MICare Database Structure and Data Procedures:

Current Status: All the networks use common data definitions, database architecture and data management protocols developed by the iCARE informatics team. Thus, the 5 databases can be easily linked using a unique coded identifier issued by the computer at the point of patient enrollment.

Data entry and transfer: MICare will consolidate and merge databases through a customized data management system (Appendix I) built around industry standard proprietary software and applications. The networks use data collection systems that are built on the same set of unified software modules addressing the standard MICare definitions and protocols. At each hospital, trained data abstractors will prospectively enter patient data using a customized data entry program (based on Visual Basic.Net) residing on the secure hospital computer network. This permits real-time data entry at different locations throughout the hospital, avoids duplication of data entry, allows immediate linkage between data from all the networks, and enjoys the secure environment of the hospital computer network. Where on-line computers are not available (as in many follow-up clinics), abstractors will enter data into dedicated computer devices (i.e. laptop computers) and upload collected data to the network. Local data will be stored in a MS Access database. De-identified data will be periodically SSL-encrypted and transferred to a central MICare database (built with MS SQL Server) at iCARE through a website.

Data Validation & Quality: There are 3 layers of validation: (a) at data entry - the data entry program alerts the user about potential errors or conflicting data; (b) after data transfer – an error checking program at iCARE is used to detect potential errors; (c) re-check – iCARE will contact sites with missing or erroneous data and data will be re-checked by site data abstractors. To ensure data quality, we will re-abstract a random 5% of charts to check reliability and reinforce standard procedure.

Data Tracking: Maternal information will be collected until death or delivery of the baby. Infant information will be collected until death or discharge from the hospital. Patients transferred to another hospital will be tracked until death or discharge. These procedures have been previously established.

(c) Privacy and Security:

Patient confidentiality will be strictly protected. At patient enrollment, a unique coded identifier will be issued by the computer. Personal identifiers will be removed (coded identifier substituted) (except date of birth and postal code) before data transfer to iCARE. Publications will only use aggregate data. Sites will not be identified except as part of a focus group that is agreed upon by all participants. Data privacy procedures conform to PIPEDA and have been verified by the BC and Ontario Privacy Commissioner's offices and legal counsel of the Ontario Ministry of Chronic Care and Long-Term Health. A Privacy Impact Assessment (Appendix A) has been conducted on our application. It was framed against CIHR Privacy Guidelines and followed Tri-Council Policy Statement guidance. The Web server and Database server are protected by firewalls in a secure environment and reside on physically separate computers. This prevents access to the database even if someone gains control of the web server. The database server is configured to only minimal and restricted types of connections from specific computers on the intranet, with no access from the internet. Both servers are "locked down" with only essential services installed and activated, and are backed up nightly to an off-site location. Data transfer will be protected using 128-bit Secure Socket layer (SSL) encryption. Users are issued User IDs and passwords.

(d) Ethics:

Ethics approvals will be obtained from all participating institutions. Data that is collected by CPN, CNN and CAPSNet are abstracted directly from patient charts with no patient contact and no patient consent is needed. Ethics approvals for CNN, CPN and CAPSNet were obtained from participating institutions and are renewed annually. For CNFUN data and data linkage, separate ethics approvals will be obtained and informed consent will be obtained from parents when subjects attend a routine assessment at 18 months corrected age at their respective neonatal follow-up clinics. Consent will include participation in the study, conduct of the various tests/surveys, and linkage of data for research.

(e) Governance and Data Access/Use:

Shoo Lee and Nicola Shaw will oversee a database manager/programmer who will maintain the database and provide informatics guidance and advice. Network directors will provide liaison with their

networks. The MICare Steering Committee will set policies on data access and use. Access to data by researchers who are not part of the MICare Team will be by application to the MICare Steering Committee, which will consider each application based on its merits and non-conflict with the research objectives of this proposal. Institutional ethics approvals are required for any project making use of MICare data.

(f)Data Items:

The MICare Database will contain the following information for all networks: (a) Basic Patient Data, (b) Outcomes, (c) Resource Use, and (d) Key Process Indicators (Appendix J).

A.10.6 Milestones

Data collection for CPN, CNN, CAPSNet and CPPRN are on-going. Data collection for CNFUN will commence 18 months after first patient enrollment on July 1, 2007, (retroactive) and continue until 36 months after the last patient is enrolled on June 30, 2009. Since all data is stored on the central servers at iCARE, data will be periodically cleaned and processed in preparation for analysis as necessary.

A.10.7 Location

The MICare Database will be located at iCARE in Edmonton, Alberta.

A.10.8 Expertise, roles and expected contributions of team members

Shoo Lee (U Alberta) is a Canada Research Chair (Tier 1) in Knowledge Translation and Healthcare Improvement and Scientific Director of iCARE. He is a neonatalogist and health economist who guided the establishment of databases for CPN, CNN, CAPSNet and CPPRN using common variables, protocols and database systems to ensure compatibility and linkage. Nicola Shaw (U Alberta) is the Research Chair of Health Informatics for Western Canada and expert advisor to Health Infoway. Lee and Shaw will direct the MICare Database and data management center. Reginald Sauvé is a neonatalogist and epidemiologist and Chairs the Canadian Perinatal Surveillance System (CPSS) for the Public Health Agency of Canada (PHAC). Saroj Saigal (McMaster) is internationally known for neonatal follow-up research. Sauvé and Saigal will direct the CNFUN Database. Robert Liston (UBC) is a perinatologist and Chair of the Maternal Health Study Group at PHAC. Laura Magee (UBC) is an internist, clinical epidemiologist and Michael Smith Foundation for Health Research Scholar. Liston and Magee co-direct the CPN. Erik Skarsgard (UBC) is a pediatric surgeon and CAPSNet Director. Bonnie Stevens (U Toronto) is the Signy Hildur Eaton Chair of Pediatric Nursing Research and CPPRN director. Network directors will provide liaison with their networks.

A.10.9 Contribution to the overall research program

The MICare Database will serve as a common resource for all the other projects in this program of research, and enables us to quantify the burden of illness associated with neurodevelopmental delay among NICU graduates and to examine causation related to therapy and non-therapy related factors.

A.11 Project 1: Variations in long-term neurodevelopmental outcomes of preterm infants

A.11.1 Project Leader and Participants

Reginald Sauvé & Saroj Saigal (Project Lead), Patricia O'Campo, Shoo Lee, Anthony Armson, Robert Liston, Laura Magee, Erik Skarsgard, Bonnie Stevens

A.11.2 Objectives

- To study how biological, sociodemographic, environmental and treatment risks interact to affect long-term outcomes, and their relationships to short-term NICU outcomes
- To study variations in long-term neurodevelopmental outcomes among Canadian NICUs
- To identify practices associated with good or poor long-term neurodevelopmental outcomes

A.11.3 Hypotheses

- There are independent and interactive effects of biological, psychosocial, environmental and clinical risk factors on long-term outcomes, and its relationship to short-term outcomes
- There exist wide variations in long-term outcomes among Canadian NICUs

- Baseline population risks account for some but not all variations in long-term outcomes

A.11.4 Approaches

Data will be obtained for analysis from the MICare Database, including baseline population risks (sociodemographic, biological, environmental), short-term NICU outcomes, clinical practices and resource use (prenatal, obstetrical, NICU, post-NICU interventions) and long-term neurodevelopmental outcomes (from CNFUN)(Appendices J, K and L).

A.11.5 Research Plan

Study Population: We will utilize data from all infants (n=1200) born at ≤28 weeks gestation and admitted to a NICU, during a 12 month period from Jul 1, 2007 to Jun 30, 2008 for this study.

Sample Size Estimates: Using the expected mean BSID score of 100±15 SD, we estimated the power to detect a significant difference if the observed mean score at a given institution differed from the expected mean score for the total sample by 10%, 15% and 20%. Table 1 shows the estimated power to detect these effect sizes for institutions expected to recruit N=50, 100 and 150 infants.

Power (1- $P_{1-\alpha}$) to detect effect by NICU size and effect size (2 sided P_α <0.01)

N per year		50	100	200
Number of NICUs		15	4	4
Effect size	10%	0.97	0.99	0.99
	15%	0.99	0.99	0.99

Therefore the study has ample power. In multivariate regression models, we expect that the power to detect differences will be greater than in the bivariate condition. While we realize that multiple comparisons are a concern when more than one analysis of the data is performed, we are not interested in the joint confidence region for all of our hypotheses at once. Rather, we are interested in them one at a time. Under these conditions, Rothman and Greenland[33, 34] argue that "multiple inference procedures ... are irrelevant, inappropriate and wasteful of information" because they produce improperly imprecise single intervals.

A.11.6 Data Analysis Methods

Objective #1: Identify independent and interactive effects of biological, sociodemographic, environmental and clinical risk factors on developmental outcomes.

Rationale: All key demographic, antenatal and neonatal risk factors, developmental outcomes and family impact are captured in MICare Database. All risk factors will be entered into respective analysis.

Analysis 1: Crude developmental and family impact outcomes of preterm infants

Descriptive and univariate analysis will be used to examine the distribution of scores for the different tests and surveys (BSID, GMCS, ASQ, HSCS-PS, BRIEF-P). Results will be compared with normative data using t-test for normally distributed data and Mann-Whitney U-test for non-normally distributed data. We will also stratify the results by gestational age, sex and sociodemographic status.

Analysis 2: Risk adjusted developmental and family impact outcomes of preterm infants

Sociodemographic, antenatal and neonatal risk profiles of subjects who did and did not consent to participation in the surveys will be compared for possible biases. Descriptive and univariate analysis will be used to examine the distribution of scores for the different tests and surveys. Risks identified from the literature include population risks (gestational age, birth weight, socioeconomic status, race), prenatal care and obstetric complications, neonatal illness severity and outcomes (intraventricular hemorrhage, bronchopulmonary dysplasia, retinopathy of prematurity, necrotizing enterocolitis, sepsis), therapy related risks and post-NICU interventions (follow-up clinic, referral to specialists, hospitalization, alternative care). Multiple regression analyses will be used to examine the independent and interactive effects of population, morbidity and therapy related risks, illness severity, and post-NICU health care utilization on outcomes scores. The general equation for the analyses is:

$$Y_{(score)} = \beta_0 + \beta_{p(population\ risks)} + \beta_{i(illness\ severity)} + \beta_{m(morbidity\ risks)} + \beta_{t(therapy\ related\ risks)} + \beta_{u(health\ utilization)} + \varepsilon$$

Multicollinearity among independent variables will be assessed using condition indices and eigenvectors. The residuals, Cook's statistics and delta-beta will be used to assess the regression model fit. The standard errors for each interaction effect will be calculated using the variance-covariance matrix of coefficients.

Objective 2: Identify variations in developmental outcomes at 18 and 36 months corrected age

Rationale: Analysis will compare developmental outcomes across hospitals at 18 months and 36 months separately. Separate analysis will examine whether outcomes at 18 months and 36 months are consistent for the same hospitals.

Analysis 1: Comparison of crude developmental and family impact outcomes among hospitals

We will tabulate outcomes, construct gestation age specific rates, generate standardized scores for each test/survey by hospital, and compare inter-hospital gestational age specific scores.

Analysis 2: Analysis of outcomes variation between hospitals

Multiple regression models will be used to examine outcome scores (BSID etc). Risk factors (population risks, prenatal and obstetric complications, neonatal illness severity and outcomes) will be entered for staged multiple regression. Dummy variables will be used for NICUs. General equation is:

$$Y_{(score)} = \beta_0 + \beta_{h1(hosp1)} + \ldots. + \beta_{hk(hospk)} + \beta_{p(population\ risks)} + \beta_{i(illness\ severity)} + \beta_{m(morbidity\ risks)} + \beta_{t(therapy\ related\ risks)} + \beta_{u(health\ utilization)} + \varepsilon$$

where hospk is a dummy variable representing individual hospitals.

This full model represents the baseline variability in population risk among hospitals. Persistence of a hospital effect indicates differences in risk adjusted developmental outcomes.

Objective 3: Identify variations in practice associated with outcomes variation

Rationale: Controversy exists about how NICU practices and outcomes, and post-NICU interventions affect long-term developmental outcomes. We will examine the data for variations in practices and possible associations with outcomes. The results might lead us to design clinical trials of efficacy that are better targeted at improving outcomes.

Analysis 1: Identification of practice differences associated with outcomes variation

Practice variables significantly associated with outcomes on bivariate analysis will be added to the above equation. Change in outcomes variation between hospitals will be noted. Significant practice variables identified by the analysis are those that account for the change in outcomes variation, and may indicate whether they are associated with good or poor outcomes. Possible practice variations include maternal transport, investigations for prediction of preterm birth (e.g., fetal fibronectin) cervical cerclage, expectant management (e.g. pregnancy prolongation), amnioinfusion for PROM, lifestyle adjustments (e.g., strict bed rest in hospital), maternal surveillance (e.g., antepartum home care), fetal surveillance (e.g., biophysical profile), maternal drug therapy (including tocolytics, antibiotics, antenatal corticosteroids, antihypertensives, $MgSO_4$, anticonvulsants, and preventative therapies for pre-eclampsia), and delivery (timing and mode). Specific questions that will be addressed are listed in Appendix K.

Study Limitations:

(a) Generalizability: This is a national study with no concerns about generalizability

(b) Misclassification: Our previous experience with NICE suggest that misclassification arising from data abstraction is very unlikely. To provide additional safeguards, we will implement abstractor training, use standard code-books, and randomly re-abstract charts for checking.

(c) Admission bias: Since all infants born at $\leq$28 weeks gestation are admitted to tertiary level NICUs, admission bias is minimized. Infants who died before admission to the NICU are not captured by this study. However, this study is intended to address outcomes of survivors.

(d) Lead time bias: We will stratify analysis by inborn and outborn status to address this.

(e) Surgical patients: Although most CAPSNET patients will be >28 weeks gestation, it is useful to integrate the CAPSNET database into CTNPC at this time because it provides a foundation for building the future and adds additional information to the study at minimal cost.

A.11.7 Milestones

Milestones for all five projects are summarized in Figure 2.

A.11.8 Location

Data analysis will be performed at iCARE (Edmonton), and at the University of Calgary, Alberta.

A.11.9 Expertise, roles and expected contributions of team members

Reginald Sauvé (U Calgary) and Saroj Saigal (McMaster) have extensive experience in epidemiology and neonatal follow-up and will direct data analysis and interpretation. Patricia O'Campo (U Toronto) is a social epidemiologist who specializes in neighborhood effects and will assist with data analysis and interpretation. Shoo Lee (U Alberta) will coordinate data access from MICare and provide neonatal outcomes input. Anthony Armson (Dalhousie) is a perinatologist who will provide maternal-fetal medicine input. Laura Magee and Robert Liston (UBC) provide perinatal input and linkage with CPN. Erik Skarsgard (UBC) and Bonnie Stevens (U Toronto) provide surgery and nursing input and linkage with CAPSNet and CPPRN.

A.11.10 Contribution to the overall research program

Within the PARIHS framework, this project provides **Evidence** about variations in outcomes, practices and resource use that will enhance our understanding of the risk interactions affecting long-term outcomes and can be used to design interventions to improve outcomes and reduce costs in Project 3.

A.12 Project 2: Virtual Research Community and Clinical Decision Support

A.12.1 Project leader and participants

Robert Hayward – Project Lead; El-Hajj

A.12.2 Objectives

This project involves three dimensions:

- Development of a virtual research community (VRC);
- Development of customized decision-support tools based on outcomes of the EPIC-II project;
- Evaluation of access to the VRC and decision-support tools as a measure of to what extent knowledge transfer is taking place.

A.12.3 Hypotheses

- Access to the VRC will increase and expand as the project continues; and
- VRC access and therefore knowledge transfer will peak once customized decision-support tools are developed

A.12.4 Approaches

This "horizontal" project complements the timelines and goals of the other projects in this application. It integrates the evidence base built up over the five years of this project in a way that supports the transfer of knowledge gained, starting with the building of a Virtual Research Community (VRC). The Centre for Health Evidence (CHE) is a multi-disciplinary, multi-institutional and multi-national initiative that brings universities and health organizations together to support the learning, teaching and practice of evidence-based health care. The CHE has extensive experience building and deploying VRCs of the type required by the overall team project. CHE currently supports similar initiatives in Canada and a number of countries worldwide.

The overall team grant project has specific needs for the design and deployment of an "infostructure" that helps investigators come together in support of the project's research goals. To do this, barriers of geography and time must be overcome. CHE provides private information spaces and early systems for gathering, organizing and sharing the vast amounts of information that are needed by leadership and administrative teams. Early information management actions are later synchronized with the vision and ultimate implementation of a fully functional virtual research community. Project 2 is about "infostructure", not "infrastructure". It therefore does not pertain to the physical construction of rooms, wires or computer hardware that may be required to access the infostructure created for the overall project.

Instead, Project 2 develops a research-focused VRC that will allow investigators and clinicians to collaborate and to share findings online. VRCs are developed at the Centre for Health Evidence, housed within the Faculty of Medicine and Dentistry at the University of Alberta, in the form of private online environments called VIVIDESK "desktops". These password-protected environments support knowledge transfer in several ways. These include the integration of Internet communications tools within desktops to facilitate exchanges among researchers separated by time and space, the development and deployment of evaluation tools, and access to best-of-breed research tools and clinical information resources.

Any desktop may include features such as virtual working group folders for sharing files, meeting minutes, contact information, customized shortcuts to key websites, and point-of-need help for every resource and tool. Internal evidence, the information created and used by researchers, can also be integrated. Each desktop is available to authorized members of that community only, which allows for protected sharing of information, ideas, and personal information. Access levels (no access, read only, editing rights) are controlled at the individual level. Custom tools for tracking research projects within the scope of this overall team project can also be developed. CHE also develops and provides online aids, such as decision-making tools, to help users formulate questions, select resources, and then appraise and apply knowledge. Because usage data is monitored and recorded, CHE also measures the impact of information use in order to gain insight into knowledge transfer activities of users. By managing evidence dissemination, embedding evidence in clinical systems, and correlating evidence presentation and integration strategies with changes in practices and outcomes, new information about effective knowledge transfer will be generated.

Early in the overall project, the most pressing need will be for communication tools like Internet conferencing and telephony tools that researchers can use. These tools will therefore be licensed and integrated into these environments for use by research team members. In addition, high-quality information resources of particular relevance to the team will be obtained and deployed in this environment. Custom tools for tracking research projects will be developed as required. Tools of relevance to NICU staff will also be made available through the same interface. This is possible while still protecting the privacy of researchers' information since user groups can be assigned to see only the areas of the VRC for which they have access authorization.

Once intervention data is available through the EPIC-II project, customized decision-support tools will be developed based on the practice guidelines developed over the course of EPIC-II. The development of these decision-support tools takes into account the reality that many hospitals do not have electronic medical records systems in place. The proposed CDSs will take the form of decision-making wizards to help researchers and clinicians make the best possible choices for patient care. That NICUs have computers on the units (ranging from about two for an entire unit to one computer for every two to three patients) will allow for the rapid dissemination of this information, not just in the form of CDS tools, but also in the form of other information (e.g. guidelines updates) that can be rapidly uploaded and accessed.

Dissemination of information from EPIC came in the form of face-to-face meetings and education sessions with NICU clinical staff. The advantage of giving NICU staff access to the VRC environment is that information dissemination does not rely on individuals being in one place in one (or various) time(s). Information access is more efficient via an online environment since it is asynchronous: users can access it according to their needs and schedules. As a result, delays in information dissemination because of such factors as nurse educator availability or staff shift work are eliminated.

A.12.5 & A.12.6 Research Plan and Methods

Phase I. The VRC will be rolled out to researchers and staff of all participating NICUs simultaneously. Researchers and staff will be placed into different usergroups for the purposes of accessing information and for gathering usage data. Usergroup divisions will be determined once it has been decided which individuals will participate in this part of the study. Once the VRC is operational, a data warehouse will be built to capture aggregate, anonymous information such as usergroup, desktop and application usage frequency, desktop and application usage duration, time (of day, week, month or year), and location of information access. The aim of this study will be to measure usage between groups of researchers and staff so as to

gauge the general level of VRC activity and knowledge transfer taking place at the point where EPIC-II is in its incipient phase. This will act as an internal control for the second phase of this research.

The basic research questions we seek to answer during this phase include the following:

1. How does application usage behavior generally vary between different usergroups?
2. Which applications do usergroups access with particular frequency?
3. What are the diurnal variations in application usage?
4. From where does application usage occur at different times of the day / week? (e.g. do users more commonly access information from within NICUs or from the outside?)

On the basis of these questions, we hypothesize that, during this phase of the study:

1. Application usage will be most pronounced among researchers as they use communications and research tracking tools to facilitate their work;
2. Usergroups will most frequently use applications that are specific to their disciplines;
3. Application access will occur mainly on evenings and weekends when researchers are not teaching and when NICU activity is generally more quiet;
4. Nurses and paramedical staff will primarily access the VRC from the workplace, while researchers and staff physician usergroups' access will occur primarily from outside the NICU.

The main data collected, analyzed and warehoused include desktop information, grouped user information, grouped and individual application information, application usage time, days of the week on which applications were accessed (including weekdays and weekends), and location from which access occurred. Usage data is stored in discrete databases, separate from identifying and demographic information about users, and data abstracted to a data warehouse is further anonymized to prevent identification of individuals.

Application of data mining tools—association rules mining[35] and decision trees[36] — will help identify frequent patterns that occur above a predefined threshold. Through this identification previously hidden but important user behaviors will be uncovered. In this particular project, we are interested in examining positive data associations across individual VRC user groups and time. In the VRC studied, we expect that participants' access will start slowly, with increases occurring as users become habituated to the system and as new tools are provided to them. Periodic variations in usage will occur depending on such factors as the time of year (for example, usage may increase among researchers during holidays when they have fewer teaching obligations). In addition, we expect to detect negative patterns of behavior: that is, behaviors indicating that specific items did not occur together. For example, we predict that some resources will not be used frequently (if at all) by participant groups to whom the applications are not targeted. This lack of use may have implications for resource licensing costs.

Phase 2: Once EPIC-II has completed the phase of developing best practice strategies for the five major morbidities targeted, custom clinical decision support tools (CDSs) will be built to support these strategies. Clinical Decision Support (CDS) systems link observations and knowledge about health to influence choices for improved health care. This second phase project manages dissemination of EPIC-II deliverables, embeds knowledge products in clinical workflow, monitors associated information behaviors and facilitates the study of evidence uptake at the point of clinical decision-making.

CDS materials will be integrated with materials dealing with patient care issues (such as patient safety) as well as with teaching, administrative and communications materials. The integration engine in the VRC will allow information from one resource (such as a patient condition in a health record) to trigger automatic presentation of information from other resources (such as evidence-based Process Care Maps). In short, the supporting VIVIDESK technology is a point-of-care distributed informatics laboratory that can record how evidence is used, and how information behaviors are affected by how evidence is embedded in clinical workflow.[37]

One more research question will therefore be added to data analysis: How does application usage change once the customized CDSs have been deployed? It is expected that VRC usage will increase

especially among usergroups for whom the customized CDSs are targeted. The general increase in VRC usage will correlate with particularly heavy access to the customized CDSs.

A.12.7 Milestones

Milestones for all five projects are summarized in Figure 2.

A.12.8 Location of research

Data collection and analysis will occur through the VIVIDESK data warehouse located at the Centre for Health Evidence, University of Alberta.

A.12.9 Expertise, roles and expected contributions of team members

Hayward is the Director of the Center for Health Evidence in the Faculty of Medicine and Dentistry at the University of Alberta. In his capacity as director, Hayward coordinates strategic information management, knowledge information management, learning information management, clinical information management and research information management. He is also an editor of the *Users Guides to the Medical Literature*, and will use his expertise in information management (strategic, knowledge, learning, clinical and research) to direct the project. El-Hajj is a Researcher and Data Architect at the Center for Health Evidence and an expert in data mining techniques. He will build the data warehouse and conduct data analysis.

A.12.10 Contribution to the overall research program

This project complements the EPIC-II project in that it evaluates the uptake of clinical research information that is developed over the course of that project. The fit with EPIC-II is iterative in that information from the VRC project will inform knowledge transfer efforts on the part of the EPIC-II team. Within the PARIHS framework, Project 2 provides the **Context** to achieve the overall goal of successful implementation of practice change. Establishment of the VRCs and development of CDC tools will support a learning culture within each hospital unit as well as empowering leaders to guide and evaluate the culture within these units.

A.13 Project 3: Evidence-based Practice Identification and Change, Version II (EPIC-II)

A.13.1 Project leader and participants

Shoo Lee – Project Lead; Bonnie Stevens, Ross Baker, Khalid Aziz, Arne Ohlsson, Keith Barrington

A.13.2 Objectives

To develop and evaluate a next generation EPIC-II model for quality improvement and knowledge translation that will target multiple outcomes simultaneously and develop comprehensive "best practice" strategies for NICU care of preterm infants, including patient safety.

A.13.3 Hypotheses

- EPIC-II improves multiple NICU outcomes simultaneously
- EPIC-II improves long-term neurodevelopmental outcomes of preterm infants admitted to NICUs

A.13.4 Approaches

This EPIC-II Study is a prospective intervention study using a modification of the original EPIC method in 3 phases. Phase 1: Year 0 data will provide baseline data for comparison with outcomes after EPIC interventions. Phase 2 (Year 1-3): all 30 NICUs will target all 5 major morbidities for improvement, and develop comprehensive best practice strategies. Phase 3 (Years 3-5): 18 month and 30 month neurodevelopmental assessments and economic evaluation will be performed, and results analyzed.

A.13.5 Research Plan

The study will be conducted at all 30 tertiary level NICUs across Canada. The large sample size is necessary because the extensive systematic review of practices and implementation of multiple practice changes targeting multiple outcomes requires a large number of centres for adequate validation. Furthermore, a large sample size will allow the study to be completed in less time and will facilitate effective knowledge translation to all centres across the country. Finally, a randomized control trial of EPIC-II is not

feasible because Canadian NICUs are not willing to be randomized to the control group after the positive results of the first EPIC study.

We will enroll all infants <29 weeks gestation (n=3600) admitted to 30 NICUs (Appendix C) from Jul 1, 2007 to Jun 30, 2008 (Phase 1 - Baseline data) and from Jul 1, 2008 to Jun 30, 2011 (Phase 2). This will provide adequate sample size to distinguish change in the incidence of the primary outcomes (survival without major morbidity, 18 month BSID and GCMS), comparing 12 months prior to, and 12 months after implementation of Phase 2.

The primary outcomes analyzed will be: survival without major morbidity (intraventricular hemorrhage, chronic lung disease, nosocomial infection with organisms, necrotizing enterocolitis, retinopathy of prematurity); 18 month BSID and GCMS. Secondary clinical outcomes include: death, individual major morbidities (as above), treatment errors, 36 month scores on Health Status Classification Pre-School (HSCS-PS), Ages and Stages Questionnaire (ASQ), BRIEF-P questionnaires. Secondary resource usages to be considered are: cost, length of hospitalization, length of ventilation, length of oxygen therapy, use of central catheters, parenteral nutrition, ECMO

Clinical outcomes will be defined as follows:

- Nosocomial infection will be defined using the Center for Disease Control criteria[38] based on the following principles: [i] combinations of clinical, laboratory and other diagnostic test information must be used; [ii] clinical diagnosis is an accepted criteria; [iii] the infection was not incubating at the time of hospital admission (defined as development of clinical signs of infection and positive blood cultures more than 48 hours after NICU admission); [iv] infection is not acquired transplacentally (defined as infections known to be transmitted primarily transplacentally, e.g. cytomegalovirus, toxoplasmosis, rubella, hepatitis B, human immunodeficiency virus); and [v] evidence of hospital acquisition is considered individually. The subgroups of babies with Gram positive (largely coagulase negative Staphylococcus) and Gram negative bacteremia, and fungaemia will be specifically targeted, given their differing presentations, complications, and resource utilization.[39]
- Necrotizing enterocolitis is defined using Bell's criteria[40]
- Chronic lung disease is defined according to Shennan.[41]
- Intraventricular hemorrhage will be classified using the Canadian Pediatric Society classification,[42] from cranial ultrasound performed during the first 28 days of life.
- Retinopathy of prematurity will be staged according to the International Classification of Retinopathy of Prematurity[43] and the Reese Classification of cicatrical disease[44]
- Treatment errors will include medication errors or other incidents reported through incident reports. Ten percent of patient charts will be randomly selected for review by a panel of 3 neonatalogist/ advance practice nurses (neonatal nurse practitioners) and the incidence compared with incident reports.

Lee et al[5,45] reported 69% incidence of survival without major morbidity among Canadian NICUs. We estimated the power to detect a significant difference if the observed NICU incidence changed by 10%, 20% and 30%. Computations are based on 12 months of data collection for all infants (assumed N) prior to, and for 24 months after implementation of EPIC-II, using a 2-sided $\mathbf{P}_{\alpha}<0.01$.

Power ((1- $P_{1-\alpha}$) to detect effect by NICU size and effect size (2 sided P_{α} <0.01)				
N per year		50	100	200
Number of NICUs		6	3	3
Effect size	10%	0.99	0.99	0.99
	20%	0.99	0.99	0.99
	30%	0.99	0.99	0.99

Data elements and key process indicators can be found in Appendices J and L, respectively. In order to collect and verify the data, we will expand the existing CNN Database data entry program to prospectively collect the additional data required for this study. Cost data for Year 3 (post-EPIC-II) will be compared with Year 1.

A.13.6 Methods

The EPIC-II project touches on all facets of the PARIHS model:[46] Evidence, Context and Facilitation. Methods are described below for Phases 1 and 2 as they pertain to each of these components.

Phase 1: Preparation (12 months data collection/preparation)

Evidence: Baseline data will be collected at all NICUs for 12 months during Year 0. Clinical teams at each site will attend a workshop to learn practical skills in critical appraisal before completing a systematic review[47,48, 49,50,51,52,53] of published literature (Cochrane Library, MEDLINE, EMBASE, CINAHAL) in target areas. The review will identify risk factors for each major morbidity and collect strategies that have been used to reduce incidence of these morbidities. From this review, each site will develop a List of Potentially Useful Practices (Appendix M), following which sites will interact to develop a single Common List of Potentially Useful Practices (Common List).

At the end of 12 months, the data will be analyzed to identify key practice differences associated with variation in major morbidities among participating NICUs. This will provide additional evidence on what practices should be targeted for change. Inclusion of pooled data from all 30 NICUs will provide sufficient power for analysis. A detailed description of associated analyses is presented below:

a. *Analysis 1: Analysis of outcomes variation between NICUs (for dichotomous outcomes)*

To take into consideration patient clustering from NICU to NICU, hierarchical logistic linear regression models will be fitted for each of the NICU dichotomous outcome variables. Variations in incidence rates of NICU outcomes, adjusted for baseline patient level risk factors, will be presented and the effect of each of the NICU level characteristics will be discussed. The following two-level (patients within NICUs) hierarchical logistic regression model will be used for each of the dichotomous outcomes, accounting for patient characteristics. Let p_{kl} be the probability of a particular response for the l-th patient in NICU k. Let $X_1,\ldots,X_M$ represent patient-level characteristics and $Z_{1\ldots}Z_Q$ the NICU-level covariates.

The general form of the hierarchical logistic regression model constitutes:

at the level I, $$\log(p_{kl}/1\text{-}p_{kl}) = \beta_{0k} + \beta_{1k}X_1 + \ldots + \beta_{Mk}X_M$$

and at the level II, $$\beta_{Mk} = \beta_{M0} + \beta_{M1}Z_1 + \ldots + \beta_{MQ}Z_Q + b_{mk}$$

Here, $k = 1, \ldots, K$, $K = 17$; m = 0, 1, …, M; b_{mk}'s are the random terms assumed multivariate normal with $E(b_{mk}\} = 0$ and $\text{Var}(b_{mk}) = \sigma^2_m$. We will implement a full Bayesian inference procedure and assume, at the level III, suitable prior distributions on the second level coefficients and on the variance components of the random terms.[54]

b. *Analysis 2: Identification of practice differences (process) associated with outcomes variation*

Practice (process) variables significantly associated with outcomes on bivariate analysis will be added to the above equation. Change in outcomes variation between NICUs will be noted. Significant practice variables identified by the analysis are those that account for the change in outcomes variation, and may be targeted for practice change intervention.

c. *Analysis 3: Analysis of outcomes variation between NICUs (for continuous outcomes)*

Continuous NICU outcomes will be analyzed respectively using hierarchical linear regression model:

$$\text{Expected } (Y_{kl}) = \beta_{0k} + b_{1k}X_1 + \ldots + \beta_{Mk}X_M$$

and $$\beta_{Mk} = \beta_{M0} + \beta_{M1}Z_1 + \ldots + \beta_{MQ}Z_Q + b_{mk}$$

and once again, a full Bayesian inference procedure will be implemented. The same process for identification of practice differences is applied.

This information will be used to revise the Common List and to assign priorities for targeted intervention.

Context: The goal of the Context portion of Phase 1 is to explore the perspectives of health care professionals on factors that influence change to policies, protocols and practices in the NICU. A mixed methods design consisting of qualitative[55] (individual and focus group interviews) and quantitative[56] (global organizational measure) components is proposed. This will be performed at the end of Phase 1.

Qualitative interviews will be conducted with health care professionals who have worked in the NICU for a minimum of 12 months and work at least 0.5 FTE. Approximately 6-8 individual interviews and

1 focus group with 6-8 participants will be conducted at each site. Participants will take part in either the individual or focus group interview but not both.

Data will be collected through interviews and a survey. Four experienced interviewers will be trained to conduct the interviews with one individual as the primary interviewer at all sites to ensure consistency across data collection. Semi-structured interviews will focus on participants' views about: existing policies and protocols dealing with identified neonatal problems (e.g. infection); the most successfully and least successfully implemented policies and protocols; and individual, unit and systems factors that influenced the implementation of practice changes on the unit. This semi-structured interview style allows participants to talk about specific events and to express their opinions on issues that they felt were particularly important. Focus group interviews will also be conducted. Interaction in a group format often leads to a different understanding of the issue[57] compared to the information derived from an individual interview.

Mayring's[58] approach to content analysis will be used to analyze the data. All audio taped interviews will be transcribed verbatim, printed and read to develop an overall sense of the data. Using inductive reasoning, the data will be organized into categories that reflect emerging themes and early coding ideas. In the second stage of the analysis, emerging themes will be revisited and the relationships between themes examined. To retain sight of the original context and meaning of the transcripts, the raw data will be revisited repeatedly during the analysis process to make comparisons, identify similarities and to observe and account for differences.[59] The data will be first analyzed separately by site (i.e. each individual NICU) and then by health condition or content group (e.g. infection). The themes and subsequent categories may be aggregated to achieve a collective perspective.

Ensuring rigor in qualitative research is about managing sources of bias.[60] Working as a team on the analyses will be a deterrent to several potential sources of bias and will provide a form of investigator triangulation[60,61], In addition, the data will be subjected to individual analyst triangulation[62] where an experienced qualitative researcher not affiliated with the study will read uncoded sections of transcripts and compare the themes that emerged from the reading of the data with themes of the original analyst to check for consistency in the results. Shortell's Quality Improvement Implementation Survey[63] (Appendix N) will be used to quantitatively examine organizational behavior/culture issues that may affect implementation of practice change in the NICU.

Each site will receive a detailed individual report on the data from the qualitative interviews and the global organization measure. The goal of feeding this data back to the individual units will be to allow each unit to further tailor their proposed practice changes to the culture of the respective units.

Facilitation: Clinical teams made up of neonatalogist, nurse educator/ advanced practice nurse/ neonatal nurse practitioner, respiratory therapist, quality improvement officer will be established at each site. Clinical teams will lead EPIC-II efforts at each site and liaise with the Steering Committee and Clinical Teams from other sites.

At a 3-day meeting, clinical teams will use the gathered evidence to develop a template of strategies for practice change. The template will contain 3 parts: clinical practice guidelines (Appendix O), a communication strategy to inform NICU staff of necessary changes, and a training strategy to teach NICU staff about new protocols.

Phase 2: Implementation of Change Strategy (3 years)

Evidence: During Phase 2, all NICUs will share collected information and experiences with the assistance of knowledge brokers. Data analysis will also be undertaken at this time to compare outcomes within NICUs and between NICUs. The analyses will be done as follows:

(a) Within NICU comparison

Analysis 1: Control charts will be used to plot quarterly outcomes/process indicator incidences.

Analysis 2: Paired t-test and Chi-square analyses will be used for intra-NICU comparison of outcomes incidence before (12 months) and after (24 months) EPIC-II implementation.

(b) Between NICU comparison

Analysis 1: Control charts will compare NICUs with high, median, low incidence of outcomes.

Analysis 2: To take into consideration patient clustering from NICU to NICU and to account for the effects of process characteristics, hierarchical logistic regression model will be fitted for each of the NICU dichotomous outcome variables. Variations in incidence rates of NICU outcomes, adjusted for patient level risk factors, will be presented and the effect of each of the NICU level process characteristics will be discussed. The following two-level (patients within NICUs) hierarchical logistic regression model will be used for each of the dichotomous outcomes, accounting for patient and process characteristics. Let p_{kl} be the probability of a particular response for the l-th patient in NICU k. Let $X_1,\ldots,X_M$ represent patient-level characteristics and $Z_1,\ldots Z_Q$ the NICU-level covariates.

The general form of the hierarchical logistic regression model constitutes:

at the level I, $$\log(p_{kl}/1\text{-}p_{kl}) = \beta_{0k} + \beta_{1k}X_1 + \ldots + \beta_{Mk}X_M$$

and at the level II, $$\beta_{Mk} = \beta_{M0} + \beta_{M1}Z_1 + \ldots + \beta_{MQ}Z_Q + b_{mk}$$

Here, $k = 1, \ldots, K$, $K = 17$; m = 0, 1, …, M; b_{mk}'s are the random terms assumed multivariate normal with $E(b_{mk}\} = 0$ and $\text{Var}(b_{mk}) = \sigma^2_m$. We will implement a full Bayesian inference procedure and assume, at the level III, suitable prior distributions on the second level coefficients and on the variance components of the random terms.

Analysis 3: Continuous NICU outcomes will be analyzed respectively using hierarchical linear regression model:

$$\text{Expected } (Y_{kl}) = \beta_{0k} + b_{1k}X_1 + \ldots + \beta_{Mk}X_M$$

and $$\beta_{Mk} = \beta_{M0} + \beta_{M1}Z_1 + \ldots + \beta_{MQ}Z_Q + b_{mk}$$

and once again, a full Bayesian inference procedure will be implemented.

(c) Group Comparisons

Analysis 1: Control charts will be used to plot incidence of outcomes at three monthly intervals to track longitudinal progress and compare outcomes.

Analysis 2: The t-test and chi-square analysis will be used to compare incidence of outcomes between the Target Morbidity and other Groups, and within Groups before and after EPIC-II

Analysis 3: Hierarchical logistic and linear regression (general equations above) will be used to compare dichotomous and continuous outcomes of NICUs in the Target Morbidity Group with those in other Groups after implementation of practice change. Persistence of a NICU effect will indicate differences in risk adjusted incidence of outcomes.

Context: Feedback will be provided every three months to NICU staff, using Control Charts[64] (Appendix P) to illustrate progress of morbidity incidences and compliance with protocols. Long-term outcomes will not be used for these cycles. An important objective of this study is to sustain enthusiasm, reinforce procedures and encourage efforts to improve practice until the changes implemented become routine. Therefore, the objective of the rapid cycles is not to statistically evaluate outcomes every 3 months but to provide feedback, reinforce procedures, encourage continued efforts, and provide an avenue for protocol revisions if unanticipated situations arise.

At a randomly selected time during each 3 monthly cycle, the NICU nurse leader will observe procedures in the NICU to monitor compliance with recommended protocols. The percentage compliance with recommended protocols will be charted using Control Charts and graphs and fed back to NICU staff.

Facilitation: Clinical Teams at each NICU will implement the Communication and Training Strategies. Communication sessions will include information sharing, structured team discussion, critique and consensus building, and input and feedback. Training will be provided for new protocols. Information packages, prominent posters, newsletters, notices, communication books, and the CNN web-site will be used to provide additional information and reinforce the need for change. The Clinical Team will be a resource for NICU staff and will address information needs, difficulties with change implementation and other concerns.

A.13.7 Milestones

Milestones for all five projects are summarized in Figure 2.

A.13.8 Location

Data collection and quality improvement efforts will occur in NICUs. Data analysis will be conducted at iCARE.

A.13.9 Expertise, roles and expected contributions of team members

Shoo Lee (U Alberta) developed the EPIC process as a scientific method for improving quality of care and will direct this study. Bonnie Stevens (U Toronto) will conduct the qualitative and quantitative studies to evaluate context. Ross Baker (U Toronto) is internationally known for his work in quality of care, patient safety, organizational culture and change, and will provide advice and direction in organizational behavior, quality improvement and training of hospital teams. Arne Ohlsson (U Toronto) is a neonatalogist and former Director of the Canadian Cochrane Collaboration and Center and will direct knowledge management and dissemination. Khalid Aziz is a clinician leader who will lead implementation of practice change in NICUs. Keith Barrington is a neonatalogist and clinician scientist who Chairs the Fetus and Newborn Committee (FNC). He will provide input and liaise with the FNC to set practice guidelines.

A.13.10 Contribution to the overall research program

This project brings together the interplay of **Evidence, Context** and **Facilitation** from the PARIHS framework to improve quality of care in the NICU microsystem environment of clinical practice. It creates a practical model for quality improvement that can be applied in any health care area, and is an effective tool for knowledge translation.

A.14 Project 4: Identify Best Practices and Develop Indicators to Improve Quality of NICU Care

A.14.1 Project leader and participants

Nicola Shaw – Project Lead; Shoo Lee, Arne Ohlsson

A.14.2 Objective

- Identify and validate indicators of quality of care that will not only monitor outcomes but also guide continuous quality improvement efforts in perinatal care

A.14.3 Hypothesis

Potentially useful practices in perinatal care can be identified by systematic reviews of the literature, and analysis of how care pathways and processes of care impact on outcome. Upon integration of the results with the best practices identified in Project 3 followed by a validation process, we expect to derive indicators of health care quality that measure both outcomes and processes of care.

A.14.4 Approach

Standardized health care quality measures (or performance measures) are vital for assessing the quality of health care. To be effective, such measures must be easily and consistently obtainable. They must measure not only health outcomes but also processes of care, organizational efficiencies and patient satisfaction. They should be easily integrated into systems used for improving the quality of health care. Unfortunately, such measures are not currently available in perinatal care. Therefore, we will take an inter-disciplinary approach integrated strongly with Projects 1, 2 and 3 in order to develop new indicators based on both best practice and the evidence available.

A.14.5 Research Plan &A.13.6 Methods

This research will be conducted in three stages, as follows:

Systematic Reviews

We will conduct systematic reviews of the published literature (including the Cochrane Library, Medline, Embase, Cinahal) to identify best practices and potentially useful practices in perinatal care, with respect to the 5 major perinatal morbidities associated with death and poor long-term neurodevelopmental outcomes (nosocomial infection, bronchopulmonary dysplasia, intraventricular hemorrhage, necrotizing enterocolitis and retinopathy of prematurity). We will specifically review the published indicators for quality

of care for children and adolescents developed by the RAND Corporation[65] and the Agency for Healthcare Research and Quality[66] in the US as these can potentially be adapted for use in Canada.

Consequently, a list of potential indicators will be developed for each stage of perinatal care including: antenatal care, childbirth, neonatal care, and neonatal developmental follow-up. The indicators will include measures of clinical outcome, process of care, organizational efficiency, and patient satisfaction. Specific attention will be paid to ensure that they capture dimensions of morbidities, patient safety, chronic disease management (as many high risk infants have long-term developmental and health problems requiring chronic disease management) and end-of-life care of very ill infants.

Derivation of Candidate Indicators:

We will integrate the results of our systematic reviews with the best practices identified in Project 3 (EPIC-II) to derive potential indicators of quality that measure both outcomes and processes of care. We will use the care pathways defined in Project 3 for each neonatal major morbidity (BPD, IVH, ROP, Infection, NEC) to identify process indicators that measure care processes at critical incident points. For example, important determinants of nosocomial infection in the NICU include handwashing, use of sterile technique for procedures, central catheter care, parenteral nutrition, skin breaks and use of mechanical ventilators. A care pathway will be defined for each of these determinants. Using these care pathways, we will identify important processes along the care pathways that can be measured and used to assess the adequacy of compliance with the care pathway.

Indicators will be selected using the following criteria:

- They must be objective, measurable, based on current knowledge and clinical experience, and reflect structures, processes or outcomes of care.
- They must be obtainable, clear, reproducible and can be used in a consistent manner.
- They must measure the outcome being tested.

Each of the candidate indicators will be tested against these criteria and the most suitable indicators will be selected by a panel of 3 experienced researchers and clinicians (the "Panel") using a modified Delphi process. We will use the Vividesk supported workspace developed in Project 2 to conduct our Delphi study remotely. Each member of the panel will be blinded to the choices of the other members of the panel. They will be asked to score each candidate indicator according to the criteria list. Results will be compiled and tabulated, and the candidate indicators will be ranked. The full panel will then review the results together, and consensus will be obtained on ranking and selecting indicators.

Validation of Candidate Indicators:

The last stage of this project is the validation of the indicators selected. The MICare Database will be used. Content validity will be assessed by the Panel through a consensus process using a modified Delphi method. Construct validity will be tested by tabulating the data from different hospitals and determining whether there are systematic differences between hospitals in the incidence of outcomes that may be potentially attributable to errors of data collection or interpretation. Concurrent validity will be tested by classifying the patients according to population characteristics and diagnostic types, and determining whether there is a logical correlation between specific patient characteristics and the candidate indicators. Consistency and reliability will be tested by determining whether the candidate indicators are consistently captured for all patients in the databases examined, i.e. what is the percentage of data that are missing, questionable or potentially erroneous. Finally, a simulation exercise will be run using data from Project 3 to determine whether changes in the process indicators over time correlate with changes in the outcome indicators. This will provide evidence for whether the process indicators selected have value in identifying problems with the care processes associated with changes in outcomes.

A.14.7 Milestones

Milestones for all five projects are summarized in Figure 2.

A.14.8 Location of research

The research will be conducted by a highly qualified research team at iCARE (Integrated Centre for Care Advancement through Research). iCARE was recently established as a partnership between the University of Alberta and Capital Health, and is designed to integrate research and health care delivery to facilitate translation of knowledge into practice and policy change. iCARE has many experienced faculty engaged in health services research, and many supporting research staff, including statisticians, epidemiologists, economists, outcomes analysts and others. Thus, iCARE is an ideal environment for conducting this research and moving it into actual practice and policy change.

iCARE will provide research space and equipment to support this research, including computers, software, telephones, fax, office supplies and other necessities.. Computer network support is provided by Capital Health.

A.14.9 Expertise, roles and expected contributions of team members

Nicola Shaw will lead this project drawing upon her research methodology and project management skills to co-ordinate the pan-Canadian Panel of experts. Shoo Lee will provide the content expertise.

A14.10 Contribution of this project to the overall research program

This project is innovative because it will develop indicators that can both measure quality of care and be used as a diagnostic tool to monitor processes of care for quality improvement interventions. The best practices and indicators derived in this project will be used in Project 3 and field tested in Project 2.

A. 15 Project 5: Prevalence functions for setting prognosis in the neonatal intensive care unit

A.15.1 Project leader and participants

KS Joseph – Project Lead, Nandini Dendukuri, Shoo Lee, Reginald Sauvé,

A.15.2 Objectives

- To develop prevalence functions and scoring systems to predict at birth the probability of short and longer term outcomes (i.e. death/disability) in infants <29 weeks gestation.
- To develop prevalence functions and scoring systems for various points (day 7, day 14, day 28, day 42) so as to update prognosis for short and longer term outcomes (i.e. death/disability).

A.15. 3 Hypothesis

Simple scoring systems based on prevalence functions and data from the Canadian Neonatal Network and related networks will improve the accuracy of prognosis setting for infants in neonatal intensive care units in Canada.

A.15. 4 Approaches

Prognosis setting in neonatology: The time of birth is a point in the life course when a physician is frequently expected to set prognosis ("Will my baby be alright, doctor?"). Although setting prognosis is typically a trivial exercise, the challenge in the Neonatal intensive Care Unit, given a very preterm, extremely low birth weight baby, can be daunting. Accurate prediction of short- and long-term outcomes is critical nevertheless. Life-sustaining treatment is not infrequently withheld or withdrawn when a newborn infant seems destined to die or to have a severe mental or physical disability. Also, a realistic foreknowledge of potential events can help parents to prepare and cope with problems their child is likely to encounter. Advances in obstetric and neonatal care in recent years have greatly influenced the 'borderline of viability' with improvements in both mortality and disability-free survival.[67,68] Providing anxious parents with information that helps in decision making at this critical juncture is exceptionally important. It is perhaps as important, if not more important, that physicians setting prognosis use reliable inputs to arrive at the 'correct' prognostic probability.[69,70]

Timing of prognosis setting: It is very necessary for prognosis setting in the neonatal intensive care unit to be repeated frequently in the days after birth. This is because survival to day 7 (and status on day 7) can dramatically alter prognosis. Also, with regard to mental and physical disability, the results of various tests

(for instance, the results of diagnostic imaging) that become available days or weeks after birth can improve the prediction of outcomes (for instance, by documenting the presence or absence of neurological injury).

A.15. 5 Research Plan

This project will use recent data (univariate, day-specific, survival curves for preterm infants by gestational age, birth weight, gender and other characteristics)[71] and standard statistical techniques to improve the setting of prognosis within NICUs in Canada. The logistic regression models will yield prevalence functions for short and longer term outcomes for infants <29 weeks gestation. These models will be updated as necessary to incorporate changes in prognosis over the coming years. The scoring systems will simplify the use of the prediction equations so that physicians can easily use these to estimate prognosis for different outcomes accurately. Aids will be developed to help parents and physicians (including scoring sheets as for prediction of coronary heart disease, see Appendix Q). Each neonatal intensive care unit will be provided with parent friendly software that will enable the estimation of prognosis for each outcome based on day of prognosis and on the input of specific predictors.

For short-term outcomes, prediction equations will be developed for the following outcomes that occur in the neonatal intensive care unit. Standard definitions will be used to define the outcomes (from the CNN SNAP project Abstractor Manual).

- Mortality: Death within 7 days after birth (early neonatal mortality) and death within 28 days after birth (neonatal mortality).
- Chronic lung disease: Oxygen dependency at 36 weeks corrected gestational age[41]
- Intraventricular hemorrhage: ventricular enlargement, periventricular echogenecity, or parenchymal echodensity/lucency, according to the Canadian Pediatric Society classification.[41]
- Retinopathy of prematurity, grade 3 or higher: This outcome will be defined according to the International Classification for Retinopathy of Prematurity[43] and the Reese Classification of cicatrical disease.[44]
- Necrotizing enterocolitis, stage 2 or higher: This diagnosis will be based on clinical signs and evidence of pneumatosis on abdominal x-ray or surgical/histopathologic evidence of necrotizing enterocolitis and will be defined according to Bell's criteria.[40]

For long-term outcomes, prediction equations will be developed for outcomes that occur during neonatal follow-up (data to be obtained from CNFUN) in order to set prognosis. The following long-term outcomes will be considered: cerebral palsy, visual deficit (blindness), hearing deficits (deafness), cognitive deficits and mortality under 3 years of age.

Predictor variables: Gestational age, birth weight (birth weight for gestational age), neonatal illness severity and diagnoses based on the results of various tests and surgical procedures will constitute potential predictors of future outcomes. Diagnoses such as intraventricular hemorrhage (and periventricular leucomalacia) will serve as outcomes in models setting prognosis at birth and will serve as predictor variables for models predicting longer term outcomes (such as cerebral palsy). The effect of serious congenital anomalies will be examined carefully in order to ascertain whether separate models need to be created for the subpopulation with anomalies (or whether effect modification terms will permit a single model to handle populations with and without congenital anomalies simultaneously). Timing of prognosis setting: Prognosis will need to be updated given survival up to successive time points. The cohort of subjects used to set prognosis at birth will be decremented appropriately (for instance, infants who did not survive to day 14 will be excluded from the prevalence function developed for setting prognosis on day 14), while all information that becomes available prior to day 14 will be used for developing the prediction equation required to set prognosis on day 14. Information that becomes available from day 2 to day 14 will not be used for prognosis setting on day 1.

A.15. 6 Methods

Sources of data: Data for developing the prevalence functions for prognosis setting will be obtained from the MICare Database, which will prospectively collect information from the 30 tertiary neonatal intensive

care units across Canada. The data includes information on demographic variables, obstetric information, neonatal illness severity, therapeutic intensity and selected outcomes. The data that will be used for creating the prevalence functions will be based on all infants <29 weeks who are admitted to the neonatal intensive care units in Canada. This information will be sufficient to develop prevalence functions for short-term outcomes that occur before and up to discharge from the neonatal intensive care unit, and for long-term neurodevelopmental and health status outcomes up to 36 months chronologic age. The information from CNN will be supplemented by information from the other Networks, namely, CPN and CNFUN.

Statistical analysis: This project will use recent data and standard statistical techniques to improve the setting of prognosis within neonatal intensive care units in Canada. The following statistical methods will establish an understanding of predictive factors for short and long-term outcomes.

Univariate analysis: Identification of predictive factors based on pregnancy complications, maternal and infant characteristics, etc, will be based on clinical understanding, the medical literature and epidemiologic principles. Continuous predictor variables (such as birth weight) will be categorized into small ranges and modeled using a set of indicator (dummy) variables.

Regression analyses: The study population will be divided randomly into two groups of equal size – a model building group that will be used to fit the prognostic model, and a validation group that will be used to evaluate the prognostic model. Multivariable logistic regression will be used to construct the prognostic models. For non-independent observations, such as the outcomes of infants from a multiple pregnancy, a generalized estimating equations approach will be used to adjust the variance appropriately.[72] Interactions terms between the predictive factors will be deployed based on clinical understanding and statistical performance. The need for hospital specific terms will be carefully evaluated (if there are differences in prognosis between centers).

A Bayesian Model Averaging approach will be used to assess the relative importance of the different risk factors.[73] The advantage of this method over p-value based model selection approaches is that it accounts for the uncertainty in the different candidate models. The final model is obtained as an average across the best fitting models according to the Bayesian Information Criterion (BIC). The regression analysis will provide the prevalence function for predicting outcomes of interest. The equation will be simplified into a scoring system as follows.

Development of the scoring system: The methodology used to develop the points system will be the same as that developed by Framingham investigators for predicting the risk of coronary heart disease.[74] Development of the point system is described in Appendix Q. A reference table developed from the simple scoring system will provide probability estimates for each point total[74] is outlined in Table KS. The predictive ability of the score will be assessed using the area under the receiver operator characteristic (ROC) curve. Analyses will be performed with SAS (SAS Institute, Cary, NC). The logistic regression models will yield prevalence functions for short and longer term outcomes for infants <32 weeks gestation. These models will be updated as necessary to incorporate changes in prognosis over the coming years.

Power considerations: The Canadian Neonatal Network collects data on more than 10,000 infants annually.[71] Within MICare, there will be 3,600 infants <29 weeks gestation [71] and this will enable the construction of a robust prediction equation. For outcomes such as neonatal death and chronic lung disease (frequency about 10% and 20%, respectively,[71] the study will have over 95% power to detect an odds ratio of 1.5, while for less frequent outcomes such as necrotizing enterocolitis and cerebral palsy, (frequency about 6% for both[71,75], the study will have over 85% power to detect an odds ratio of 1.5. All calculations assume an alpha level of 0.05 and a 50% frequency of the predictor (as with gender). These are relatively conservative assumptions - use of multiple years of data and inclusion of infants with congenital anomalies (even with half the data set aside for model validation) will result in higher levels of power in general.

A.15. 7 Milestones

Specific milestones for Project 5 are given in Figure 2.

A.15. 8 Location of research

Development of the prevalence functions for prognosis setting will be conducted at the University of Dalhousie in coordination with the iCARE centre.

A.15. 9 Expertise, roles of this project to the overall research program

KS Joseph (Dalhousie) has expertise in perinatal epidemiology, infant prematurity and community health. He is an internationally recognized perinatal researcher and is the driving force behind the Fetal and Infant Health Study Group of the Canadian Perinatal Surveillance System. He contributed to *The State of Perinatal Health in Canada: An Overview,* a Health Canada publication that led to changes in policies and practices in the health system. Nandini Dendukuri is a medical scientist and assistant professor at McGill University. She has research expertise in clinical epidemiology, community studies and biostatistics. She will provide her statistical expertise for both consultation and analysis of data collected by CNN based on information supplemented by CPN, CAPSNet and CNFUN. Shoo Lee and Reginald will provide expert input and access to the MICare Database..

A. 15. 10. Contribution of this project to overall research program

Within the PARIHS framework, Project 5 provides **Evidence** to create and translate knowledge. Project 5 is expected to enable more accurate prognosis setting by physicians and more informed decision making by parents.

Project 5 complements Project 1. The linkage between the networks established by the MICare database in Project 1 will expand the longitudinal dimension of the follow up for each infant and make available a large number of antenatal predictor variables (i.e. detailed information on pregnancy complications) and clinically important longer term outcomes which will permit the creation of prevalence functions for a number of conditions including cerebral palsy, blindness, and deafness.

B. BACKGROUND

B.1 Importance of Preterm Infants and Their Long-term Neurodevelopmental Outcomes

Preterm birth is the leading cause of neonatal deaths and is the most important perinatal problem in industrialized countries today[10,76] . In Canada, the incidence of preterm birth increased 30% between 1981-83 and 2004[10,77,78] and it is currently the leading cause of cerebral palsy. Lee et al[5] reported that preterm infants <1500g birth weight had significant mortality (13%) and morbidity, including chronic lung disease (26%), severe (grade 3 or higher) intraventricular hemorrhage (10%), severe (stage 3 or higher) retinopathy of prematurity (11%), nosocomial infection (22%) and necrotizing enterocolitis (7%). At 18 months of age, the National Institute of Child Health and Human Development reported that 25% had abnormal neurological development, 37% cognitive impairment, 29% motor impairment, 11% hearing impairment, and 9% visual impairment.[79] Among older children, Saigal et al and others[80,81,82,83] reported significant learning disabilities, educational difficulties and behavioral problems and up to 34% repeated a grade. Thus, long-term neurodevelopmental problems are common among very preterm infants, and the number of disabled infants has increased with the increased incidence and survival of preterm infants.

The costs of preterm birth affect not only the infant, but also their families and society. Adverse emotional effects have been observed in parents and siblings of very preterm infants and there is a 32% mean decrease in family income.[83,84,85] Although infants born at less than 29 weeks gestation comprised only 19% of NICU infants, these preterm infants accounted for 46% of NICU cost expenditures.[86] Furthermore, preterm infants consume significantly more health and educational care resources then normal term infants during their first 8 years of life.[87] It has been estimated that the incremental cost to the US education system of very preterm infants exceeded US$700 million a year.[88]

Socioeconomic and demographic risk factors reported to be associated with preterm birth and adverse infant outcomes include low maternal age and education, single marital status, black or aboriginal race, poor maternal nutrition, high parity and lack of prenatal care[10]. Perinatal risk factors include: smoking, drug or alcohol use, breech presentation, intra-uterine growth restriction, cord prolapse, preterm premature

rupture of membranes, chorioamnionitis and maternal health conditions (diabetes, hypertension and anemia, and complications at birth)[89]. Neonatal risk factors include: 1) biological factors such as low birth weight and gestation, male sex, low Apgar scores, high illness severity, bronchopulmonary dysplasia, hyperbilirubinemia, hypoglycemia, nutritional deficiencies, intraventricular hemorrhage, and treatments with potential complications (e.g. assisted ventilation, methylxanthines, glucocorticoids); 2) social factors such as family cohesion, financial burden, and parental stress and anxiety; and 3) environmental factors such as noise, bright light, pain and the availability of educational and social supports, access to health care, and early screening and intervention programs[90].

New evidence suggests that white matter injury in the brain of very preterm infants may be related to factors such as infection, systemic illness and clinical factors, including treatment with postnatal dexmethasone and indomethacin[91]. Synnes et al[6] reported that severe intraventricular hemorrhage in very preterm infants was associated with treatment factors, including vaginal delivery, lack of antenatal corticosteroid treatment, and treatment for acidosis and hypotension. Thus there is emerging evidence that neonatal clinical practices can affect long-term neurodevelopmental outcomes, which are the most important and relevant outcomes for preterm infants because of their long-term impact on health of the infant, impact on family and costs to society. Our proposed MICare Database will provide a unique opportunity to examine how sociodemograpic, environmental, biological and clinical risk factors interact to affect long-term neurodevelopmental outcomes, and may provide insights into how to design interventions to improve long-term outcomes.

B.2 Quality of Care Improvement & Knowledge Translation - Current State of Knowledge

Traditional approaches for improving quality of care are based on one or some of the following:

B.2.1 Expert Opinions and Practice Guidelines

Clinicians traditionally base practice on experience, published evidence and expert guidelines. However, individual experience is limited in scope, published evidence is often incomplete, and practice guidelines are seldom based on data from the population concerned. Even when practice guidelines are comprehensive, many clinicians do not follow guidelines. For instance, Lee et al[28] reported that only 4 of 17 Canadian tertiary hospitals adhered to national guidelines for routine screening of retinopathy of prematurity. Expert opinions and practice guidelines recommended by experts are often inaccurate because they are seldom based on good data. Emulating practices of reputable institutions is often inappropriate.

B.2.2 Making Evidence from the Published Literature More Readily Accessible

Clinicians and decision makers use information from the published literature to improve quality of care and guide policy. However, the volume of published literature has become so large that many individuals find it unmanageable. The Cochrane Library makes information more readily accessible by systematically summarizing the published literature.[48,48,49,51,52,92] However, systematic reviews are limited by lack of available reviews, poor quality of the published evidence for conducting systematic reviews, and exclusion of evidence that do not derive from randomized controlled trials (i.e. observational data). Even if the published evidence is readily accessible, providers may not necessarily access them or adopt evidence based practices. Organizational attributes are thought to influence strategies aimed at promoting evidence based practice.[93,94,95] Investigators have shown that combinations of interactive interventions and user-friendly decision support tools are most effective for increasing evidence-based practice.[96,97] Systematic methods for changing provider behavior and overcoming organizational barriers (e.g. accountability, audits, reminders, standards, incentives) are needed.

B.2.3 Using Interactive Decision Support Tools

Interactive interventions that utilize computer technology to offer decision support tools to practitioners have been shown to be effective at influencing behavior and practice patterns.[98] Hayward et al[99] has demonstrated the utility of computerized knowledge management systems that facilitate access to literature and provide tools to guide medical decision making based on evidence. An example of this is the VIVIDESK™ technology[100] that combines a computerized knowledge management and decision support tool with a virtual community of users to enhance mutual learning and support. These systems can also be

used to examine patterns of use by practitioners, which can provide insights into how best to design these systems to optimize their use and decision making by practitioners for improving quality of care.[99]

B.2.4 Continuous Quality Improvement (CQI) Methods

Continuous Quality Improvement (CQI) strategies offer another form of learning and incorporating knowledge into clinical care. Berwick[101] refers to CQI as "real time science" that can examine "the processes at work" to identify changes that might improve outcomes. Consequently, CQI can be a "better and more efficient way to learn" than prospective randomized controlled trials in some circumstances. Nolan's CQI model[102,103,104] uses repeated cycles of action and reflection. In this model, local experts examine potential improvements to their existing practices and conduct iterative learning cycles. During each cycle, they plan a test of change, do the test, study the results, and act based on what was learned (PDSA cycles). The Rapid Cycle Improvement Model[105,106] is a variant that emphasizes creation of a culture of continuous re-appraisal by using rapid PDSA cycles of short duration to make small gains rapidly and give frequent feedback regarding progress of the effort and resultant outcomes. Pace is crucial because each cycle is informative and provides a basis for further improvement. The emphasis is not on demonstrating improvements after each short cycle, but to encourage re-appraisal and reinforce procedures. The effectiveness of CQI methods was demonstrated by 10 Vermont-Oxford Network NICUs,[106,107] which used CQI to achieve 24% reduction in the incidence of infection, with annual cost savings of $2.3 million per NICU. However, the drawbacks of CQI methods are that they are subjective, use a "hit-or-miss" strategy, are sometimes not evidence-based, seldom utilize data from the institutions in question, and their results cannot be easily generalized.

B.2.5 Evidence-based Practice Identification and Change (EPIC)

To address the deficiencies of CQI methods, Lee et al[108] developed the EPIC method. EPIC introduces scientific objectivity to traditional CQI methods, focuses efforts on interventions with identified effect to maximize impact, and is more meaningful for individual NICUs. It uses an interactive and multifaceted process that involves interdisciplinary teams to harness the collective expertise of a national network of experienced clinicians, researchers and administrators, and incorporates organizational behavior and process change as part of its change strategy.

Q. What is EPIC?

EPIC is a new scientific way for translating knowledge into better quality of care. EPIC has 3 key features:

(a) Systematic review of evidence in the published literature.
(b) Quantitative analysis of outcomes and practice data to identify specific practices associated with outcomes variation for targeted intervention
(c) Utilize the collective expertise of a multi-disciplinary network of clinicians and quality improvement experts, in an on-going national effort to continuously re-evaluate, change practices and improve care.

Q. How does EPIC differ from traditional CQI Methods?

1. EPIC establishes a national system for on-going efforts to improve quality of care.
2. EPIC uses benchmarked data from the NICUs involved to identify key practices for targeted intervention
3. EPIC creates a Template for Change that can be generalized to NICUs because it is derived from an industry-wide database.

Q. Is there any evidence that EPIC works?

In a recently completed cluster randomized controlled trial of 12 NICUs, Lee et al[27] reported EPIC improved both outcomes and processes of care (e.g. nosocomial infection incidence was reduced by 40%; chronic lung disease was reduced by 20%; average time for surfactant administration was reduced from 3 hours to less than half an hour). Thus, EPIC-II is effective at quality improvement and knowledge translation. Publication of a peer-reviewed manuscript is in progress.

B.2.6 EPIC – the next step in quality improvement

EPIC conforms to the time-honored CQI principle of targeting one outcome at a time. However, the EPIC study observed that interventions targeted to improve one outcome may affect another outcome[27] (i.e. when chronic lung disease was targeted, both chronic lung disease and nosocomial infection decreased).

This suggests that it may be possible to target more than one outcome at a time. In this proposal, we have developed EPIC-II as a next generation model to target multiple outcomes simultaneously. This will permit efficient and effective development of comprehensive "best practices" for NICU care.

B.3 Using Indicators to Sustain Quality Improvement

Indicators have been used to measure various outcomes of interest, such as neonatal and infant mortality. While these indicators provide a measure of how well an institution or region is doing with respect to the outcome in question, they reveal little about how to address the quality of care or improve outcomes. Process measures provide better insight into whether the care provided is achieving the desired compliance and quality of application. Consequently, a carefully chosen combination of outcome and process indicators can potentially enable a manager to monitor outcomes and identify interventions needed to improve quality of care on an on-going basis.

B.4 Counseling Parents and Decision Making

Counseling of parents is an essential and necessary part of the care of preterm infants. Parents of preterm babies worry about whether their baby will survive, and whether there will be physical or mental handicaps that are long lasting. At present, physicians counsel parents about the prognosis of their baby at the time of birth, using survival charts and tables showing probability of mortality and morbidity based on the gestational age of the baby at birth. However, the probability of adverse outcomes changes with each day survived and with the changing condition of the baby. Unfortunately, there are currently no tools available to physicians to re-assess prognosis of the baby after birth. Consequently, parents are not properly informed and may receive conflicting information about prognosis from different practitioners, which confuses them even more and raises anxiety levels unnecessarily. There is an urgent need for tools to address this deficiency.

C. ADVANTAGES OF A TEAM APPROACH

Through the synergy of the five projects described in this proposal, the MICare Team will optimize the three key parameters of the PARIHS model (Evidence, Context, Facilitation)[46] to maximize the success of practice change implementation. Although each project will independently contribute to improving healthcare delivery for preterm infants, together the projects will add value and enable ongoing quality improvement efforts. Furthermore, the system that provides care for pregnant women, infants and their families involves a broad spectrum of healthcare professionals. It follows, thus, that change and improvement to that system of care should be led by a diverse team with expertise in a wide variety of fields. Our team includes members with expertise in neonatology, healthcare economics, knowledge translation, biostatistics, health informatics, epidemiology, nursing, and qualitative research.

Another unique feature of the Team is that researchers and end-users of the research findings are integral to the research team, research plan and organizational structure in all phases of the research. In this model, clinicians provide important clinical insight to identify the appropriate questions and factors that should be examined for quality improvement, researchers provide the expertise to examine the evidence and tease out the necessary ingredients for practice intervention, and administrators provide the resources and support for establishing practice change strategies. Then, clinicians implement the changes, researchers evaluate the impact, and knowledge dissemination to professional bodies, policy makers and the community is conducted by representatives from these bodies. Thus, the knowledge translation cycle is complete. This model allows us to identify key questions that are truly relevant and critical to improving care and outcomes, incorporate all necessary perspectives into the project design, and ensure integration of both the research and health care dimensions so that the research output is relevant, usable and desirable to end-users.

The team will also build a unique national maternal-infant database as a common resource. This adds value because all the projects utilize this resource, which increases efficiency and decreases the costs of research. It also achieves the elusive goal of establishing a standardized neonatal follow-up database for all of Canada. This will provide a firm foundation for future research that utilizes neonatal follow-up outcomes. It will also open up tremendous opportunities for research by linking population based information from the perinatal through the neonatal and infant periods.

The MICare Team builds upon the highly successful and productive NICE research team and brings together researchers from many disciplines that are complementary and relevant to this research program. Team members are experienced in collaborative research and have strong track records of peer-reviewed grant funding, publications and knowledge translation. As this proposal is a large undertaking, Shoo Lee will commit half his time (20 hours/week) to it. Although he presently participates in 17 projects, 9 of these will terminate in 2008, and 2 more are infrastructure or training grants that require minimal time commitment. The remaining projects require a total of 7 hours/week in time commitment. Consequently, he will have sufficient time for this proposal. Other team members will also contribute significant time commitment, including 10 hours/week for Project Leaders and 5 hours/week for others.

D. TRAINING

D.1 Training Plan

Our CIHR Team in Maternal-Infant Care will provide tremendous opportunities for training and mentorship, including: (a) Training Committee & Mentorship - We will assemble a Training Committee to oversee the establishment of a unique training environment. This will include 1:1 mentorship with an assigned mentor for their project, and annual interviews with the Training Committee to provide feedback and recommendations; (b) Participation in research projects – trainees will actively participate in all phases of the research projects, including design, conduct, data analysis and interpretation, manuscript writing and publication, dissemination of information, and implementation of practice and policy change. They will receive on-the-job training from their project supervisors, assume leadership roles as appropriate and interact closely with other trainees and collaborators on a daily basis; (c) Formal training and coursework – either through degree programs or through courses conducted by CIHR-funded Strategic Training Initiatives, e.g. NICE Training Program, Canadian Child Health Clinician Scientist Program (CCHCSP), Strategic Training Initiative for Research in Reproductive Health Sciences (STIRRHS), and Maternal Fetal Newborn Training Program (MFN), PhD seminar on knowledge translation offered by Dr Carole Estabrooks at the University of Alberta; (d) VIVIDESK technology™ - We will organize monthly virtual workshops using VIVIDESK™ technology, between trainees and researchers to discuss research issues and methodologies according to a structured curriculum; (e) Annual workshop and conferences – we will establish an annual workshop for Team members and collaborators, for discussing on-going and new research projects, sharing data and presenting results. Trainees will be required to attend the workshop and a trainee session will be held to discuss and share training issues. We will also sponsor trainees to attend other appropriate national and international conferences to present their research findings; (f) Funding – we will set aside almost $200,000 annually for funding studentships at CIHR recommended rates, with matched funding from NICE, MFN and STIRRHS. Additional funding may be available through other specific research projects and training grants. A Training Committee will set eligibility criteria and select applicants on the basis of merit. Trainees currently proposed by the applicants include 1 post-doctoral fellow (Xiangming Qiu), 1 PhD graduate student (Jianqing Liu) and one Pediatric Resident (Matthew Hicks).

D.2 Inter-disciplinary Training Opportunities and Interactions

Trainees that belong to the MICare Team will have many opportunities for inter-disciplinary training. Each project requires researchers from multiple disciplines (including epidemiology, statistics, geography, economics, policy, informatics, sociology, quality of care, systematic reviews, qualitative research, perinatology, neonatology, developmental pediatrics, surgery, nursing and knowledge translation) to interact and work together to analyze and interpret data. Therefore, trainees will be able not only to observe these interactions but also to participate in them, and understand how the different disciplines interface to add their particular expertise to solve the puzzle. They will utilize a variety of settings to do this, including face-to-face group discussions, teleconference, e-mail and other electronic media. They will also collaborate to write manuscripts and experience how other disciplines work. Finally, they can participate in trainee seminars conducted by MFN, STIRRHS and CCHCSP on inter-disciplinary research.

E. ORGANIZATIONAL ASPECTS, INTERACTIONS AND COMMUNICATIONS

E.1 Administrative and Operational Structures, Roles and Responsibilities

E.1.1 Coordinating Center: will provide leadership and administrative infrastructure, including coordination of research activities, organization of trainee awards, and communications, reports and manuscripts. Shoo Lee (Team Director) will have executive responsibility for MICare Database. He will be assisted by a Coordinator and will supervise the Data Analyst and Knowledge Broker at iCARE. Dr Nicola Shaw will supervise the Data Manager/Programmer and oversee the MICare Database. The Knowledge Broker will facilitate communications and knowledge transfer activities within and between sites.

E.1.2 Steering Committee: Shoo Lee (Chair), Reginald Sauvé, Robert Hayward, Nicola Shaw and KS Joseph will approve MICare policies and meet every 3 months. They will oversee operations of MICare, including planning, decision, making and resource allocation.

E.1.3 Advisory Committee: of partners and external experts will advise the Steering Committee. Members include Elaine Orrbine (CAPHC), Corrine Frick (PPP), Catherine McCourt (CPHA), Dr Gabriel Escobar (Research Director, Kaiser Permanente), Dr Adolf Vals I Soller (Director, European Neonatal Network), and Dr Brian Darlow (Australia-New Zealand Neonatal Network).

E.1.4 Project Leaders: The project leaders are Saroj Saigal & Reginald Sauvé (Project 1), Rob Hayward (Project 2), Shoo Lee (Project 3), Nicola Shaw (Project 4) and KS Joseph (Project 5). They will coordinate project activities, promote linkages between project members, liaise with the Steering Committee, monitor progress, set schedules, control expenditures and oversee data analysis and interpretation, and publications.

E.1.5 Research Networks Administration: Shoo Lee (CNN), Laura Magee (CPN), Eric Skarsgard (CAPSNet), Reginald Sauvé & Saroj Saigal (CNFUN) and Bonnie Stevens (CPPRN) will direct the 5 research networks. They will each supervise a Network Coordinator, who will maintain communications with participating sites, coordinate research projects, ensure quality of data collection and analysis, organize annual workshops and meetings, develop and send reports and newsletter updates to constituents, and act as catalyst for knowledge translation efforts at hospitals, health authorities and government agencies. Each hospital participating in a research network will have a designated site representative who will supervise a site coordinator and liaise with the Network leadership, and participate in discussions about network policies and research projects.

E.1.6 Training Committee: Anthony Armson (Chair), Keith Barrington, Patricia O'Campo and Bonnie Stevens will set eligibility criteria and make trainee selections. Potential graduate students will apply through a formal process to the selection committee. Several potential trainees have been identified. The committee will also develop the training program in coordination with out partner STIHR training programs and graduate degree programs.

E.2 Communications and Knowledge Exchange

A Core Knowledge Broker will be responsible for communications among team members and with the user community. S/he will facilitate information exchange through quarterly newsletters, face-to-face meetings, teleconferences and e-mail. S/he will keep abreast with research developments and disseminate information to ensure that team members are kept up to date. Site Knowledge Brokers will do the same at their respective sites and liaise with the Core Knowledge Broker. We will establish a website to provide current information. An annual workshop will be held for Team members and trainees to present research progress and findings, and discuss future plans. International partners will be invited to attend and contribute to the discussions. The Steering Committee and Project groups will provide regular updates of progress and new developments through the quarterly newsletter and on the website. Communication will also be facilitated among research sites by the virtual research community online tools (Project 2).

E.3 Dissemination of Research Findings

Results will be published in peer-reviewed journals and presented at scientific meetings. Reports will be distributed to relevant Canadian hospitals. Each hospital has a site investigator who is the liaison member with their respective research network (CNN, CPN, CAPSNet, CPPRN, CNFUN). S/he will work with each hospital to ensure uptake of knowledge and implementation of practice change so that knowledge translation can occur industry-wide throughout Canada on a timely basis. A knowledge broker will work

with site representatives (including site knowledge brokers) and hospital staff to facilitate practice change. The knowledge broker will develop and distribute training modules for use in future EPIC-II projects. Regular newsletters will provide updates and information. We will conduct an annual workshop to share results with clinician leaders and administrators from relevant Canadian hospitals. The aim of the annual workshops will be to share results, provide updates on advances in quality improvement research and evidence, and to conduct teaching courses on the "how to" of quality improvement. On-going analysis of the data collected in the national network databases will provide feedback to hospitals about their outcomes and practices relative to other hospitals and their progress at change implementation. We will also create a web-site so that results, knowledge, training materials etc can be readily accessed for wide dissemination. Team members who are members of key professional bodies (CPS, SOGC, CAPS, CAPHC), regional and federal health agencies (PPO, CPSS, PHAC, Health Canada), and community agencies (FRP Canada) will provide information about research findings to these bodies and work with them to implement practice guideline and policy changes. A full report will be published and disseminated at the conclusion of the study. Thus, the whole program is cohesive, inter-linked, highly integrated and has an effective knowledge transfer plan.

F. INSTITUTIONAL SUPPORT AND PARTNERSHIPS

This program of research is supported by 30 hospitals across Canada. They provide significant in-kind contribution to the cost of data collection for CNN ($180,000), and for time spent on the study (EPIC-II) by doctors, nurses, hospital quality improvement personnel and others ($1.56 million). This is a significant in-kind contribution and investment on their part. Another $60,000 worth of in-kind value will be derived from data being collected by on-going CIHR studies that will be used in this study. iCARE at the University of Alberta is the coordinating center and database center for the Team and fully supports this proposal. iCARE was recently established by the University of Alberta, Capital Health Authority and Alberta Health & Wellness as an integrated research center that brings together researchers, clinicians, decision makers and policy makers to conduct research to address health care problems and improve patient outcomes. iCARE will provide office space for Coordinating Center staff, computer support (server, networks, network support, data backup etc), internet access, communications infrastructure (telephone, fax, video-conference facilities) and financial accounting management. The Center for Health Evidence at the University of Alberta will support the efforts of Project 2, including providing space for graduate students and computer facilities needed.

F.1. PARTNERS

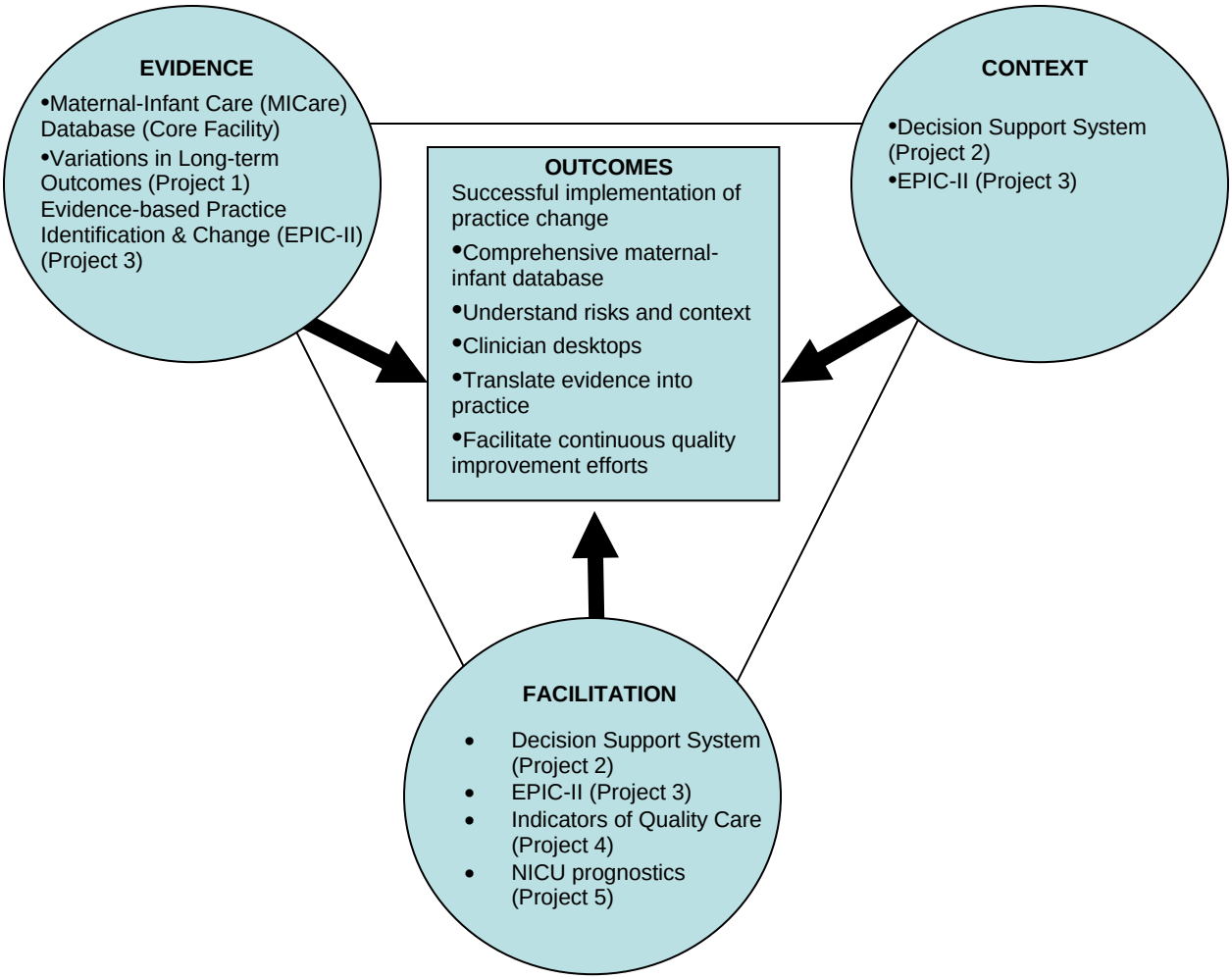
F.1.1 Governance and Management

Partners will be part of the Scientific Advisory Committee that will advise the CIHR Team in Maternal-Infant Care on its continuing objectives, activities and progress, and provide linkage with stake holders (see Section E.1.3)

F.1.2 Involvement and Commitment

Several investigators are members of key professional practice guideline committees (e.g. Skarsgard – CAPS) and will work with the committees to implement research results into guidelines. Elaine Orrbine (CEO, CAPHC) and Michele Lahey (Chair, CAPHC) will provide reports from the team to senior hospital management through the CAPHC and obtain support for the project, including contribution of time spent by doctors, nurses, allied health professionals, procurement of hospital supplies etc for quality improvement in Project 3, and to receive and implement the recommendations from the team for re-organization and resource allocation for neonatal-perinatal care regionally. We will share reports with regional and provincial health authorities. PHAC will contribute time spent by Reginald Sauvé (Director of CPSS) and Maureen McCourt to participate in policy and resource allocation discussions and engage the federal government in translating research findings into appropriate maternal and newborn health policies. In addition, all NICUs have strong parent groups and we will work with them to ensure that the public is appropriately informed. In all these activities, a knowledge broker and coordinator from each of the 5 networks will work with partners to ensure good communication and group interactions.

Figure 1: Working Model of Practice Change



Developed from:
Rycroft-Malone J. The PARIHS Framework – A Framework for Guiding the Implementation of Evidence-based Practice. J Nurs Car Qual. 2004;19(4): 297-304

Figure 2: Milestones

	Year 0 – 2007	Year 1 - 2008	Year 2 - 2009	Year 3 - 2010	Year 4 - 2011	Year 5 - 2012
Core Facility	-Enrollment of preterm infants (<29 weeks) born in Canada from July 1, 2007, to June 30, 2010 – Years 0 – 2 for CNFUN -Ongoing data collection: CNN, CPN, CAPSNet, CPPRN			-Link CNN, CPN, CAPSNet, CPPRN and CNFUN		
			-18 month follow-up			
				-36 month follow-up		
Project 1		-Identify (MICare): *Developmental outcomes risk factors f *Practice variations that influence outcomes				-Evaluate developmental outcomes at 18 and 36 months
Project 2		-Conduct needs analysis -Develop VRC for project research team and NICU staff -Build a data warehouse to collect data captured from VRC	-Evaluate Year 1 usage data -Build decision support tools (CDSs)	-Deploy CDSs -Measure access and refine CDSs based on revised clinical practice guidelines developed during EPIC-II	-Evaluate usage data recorded by VRC from one year before and one year after the EPIC-II interventions began	-Complete evaluation of VRC access -Refine CDSs
Project 3	-Baseline data collection -Systematic review	-Identify key differences in practice associated with variation in NICU infection rates -Comprehensive outcome improvement interventions		-On-going data analysis and interpretation -30 month follow-up completed		
Project 4					-Systematic reviews -Develop indicators -Authenticate indicators and validate against MICare	
Project 5			-CNN file -Short-term outcomes assessment using MICare	-Short-term analyses and modeling -Define terms for long-term outcomes	-Long-term analyses -Disseminate scoring system to Canadian NICUs	

Table 1. Scoring system using routinely by physicians in Canada to estimate the 10 year risk of coronary heart disease. An individuals profile (i.e., gender, age, etc) are used to determine a total risk score and the risk of coronary heart disease is then read off the bottom chart.

Model for estimating the 10-year risk of coronary artery disease in a patient without diabetes mellitus or clinically evident cardiovascular disease, using data from the Framingham Heart Study[a]

MEN

Risk factor	Risk points				
Age group, yr					
20–34	–9				
35–39	–4				
40–44	0				
45–49	3				
50–54	6				
55–59	8				
60–64	10				
65–69	11				
70–74	12				
75–79	13				
	Age group, yr				
Total cholesterol level, mmol/L	20–39	40–49	50–59	60–69	70–79
< 4.14	0	0	0	0	0
4.15–5.19	4	3	2	1	0
5.20–6.19	7	5	3	1	0
6.20–7.20	9	6	4	2	1
≥ 7.21	11	8	5	3	1
Smoker					
No	0	0	0	0	0
Yes	8	5	3	1	1
HDL-C level, mmol/L					
≥ 1.55	–1				
1.30–1.54	0				
1.04–1.29	1				
< 1.04	2				
Systolic blood pressure, mm Hg	Untreated	Treated			
< 120	0	0			
120–129	0	1			
130–139	1	2			
140–159	1	2			
≥ 160	2	3			

Total risk points	10-year risk, %
< 0	< 1
0–4	1
5–6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
≥ 17	≥ 30

10-year risk: _____ %

WOMEN

Risk factor	Risk points				
Age group, yr					
20–34	–7				
35–39	–3				
40–44	0				
45–49	3				
50–54	6				
55–59	8				
60–64	10				
65–69	12				
70–74	14				
75–79	16				
	Age group, yr				
Total cholesterol level, mmol/L	20–39	40–49	50–59	60–69	70–79
< 4.14	0	0	0	0	0
4.15–5.19	4	3	2	1	1
5.20–6.19	8	6	4	2	1
6.20–7.20	11	8	5	3	2
≥ 7.21	13	10	7	4	2
Smoker					
No	0	0	0	0	0
Yes	9	7	4	2	1
HDL-C level, mmol/L					
≥ 1.55	–1				
1.30–1.54	0				
1.04–1.29	1				
< 1.04	2				
Systolic blood pressure, mm Hg	Untreated	Treated			
< 120	0	0			
120–129	1	3			
130–139	2	4			
140–159	3	5			
≥ 160	4	6			

Total risk points	10-year risk, %
< 9	< 1
9–12	1
13–14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17
23	22
24	27
≥ 25	≥ 30

10-year risk: _____ %

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