Very preterm infants in Alberta: comparison of health technology service use, health outcomes and costs across five health zones.

by

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Abstract

Very Preterm Infants (VPI) (<1500g or below 32 weeks gestational age) account for only 5% of all births, but roughly half of all infant and perinatal mortality. Their high level of acuity requires extensive healthcare services during the first year of life, which result in long lengths of stay and the usage of neonatal intensive care units (NICUs). The objective of this study is to measure and compare mortality, length of stay, inpatient costs, and NICU utilization across Alberta's health zones.

The data came from the Alberta Perinatal Health Program's comprehensive list of births in Alberta from 2004-2009. This data was merged with the Discharge Abstract Databases and several smaller databases in order to retrospectively examine costs, health outcomes, and service usage of infants born or admitted to any Albertan hospital. Nonlinear regression was used to assess temporal and inter-health-region mortality rates, and a negative binomial regression was used for length of stay data.

Length of stay variation by health zone had little clinical significance, but differences in mortality rates and service utilization were significant and widely apparent. One year mortality rates between Calgary and Edmonton were 11.6% and 15.4% respectively, with Calgary having much lower mortality rates in infants at extremely low gestational ages (<25 weeks). 82.3% of VPI were born as recommended at a level three NICU facility, with 6.5% being transferred from lower level hospitals. The yearly total inpatient costs (2009 $ values) for VPI were $52 million, which averaged to $94,000 per VPI, with significant variation between health zones. The study found the current NICU allocation in Alberta to be allocatively efficient when evaluated on accessibility and bed limitations. However, statistically significant findings indicate metro locations such as Calgary and Edmonton have lower mortality rates ($p<0.05$). Future research should further explore the observed metropolitan protective relationship, and the potential role differing clinical practices in each health zone have on health outcomes and costs.

Preface

This thesis is an original work completed by Sean Tiggelaar. The research project of which this thesis is a part, received research ethics approval from the University of Alberta, as "AlbertaHOPE Study", ID. Pro 00051086, on September 30, 2014.

Dedicated to my nephew Owen (2013 – 2015)

Though his years were few, his struggle with MECP2 duplication syndrome taught me much about the togetherness of family, the depth of love and the vital importance of research. Reflection upon his short life has made me want to strive to improve and touch the lives of others through research.

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Soli Deo Gloria

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1 INTRODUCTION

1.1 Preterm Infants

Preterm infants are defined as newborns born before the full term pregnancy period of 37 to 42 weeks gestational age (GA). This occurrence is anything but new, as preterm birth globally affects 15 million newborn infants every year[58]. Globally, rates of prematurity greatly fluctuate by country, this is in part due to a country's maternal health, reproductive technologies, healthcare services, and population demographics. In developed countries rates are much lower, with prematurity estimated at 7.5% of births, but current research indicates that the rate is rising[52]. Canadian rates appear slightly higher as 8% of all live in-hospital births in 2009-2010 were born preterm[27]. In Alberta preterm birth rates have fluctuated greatly, sitting at 8.3% in 2001 and reaching a high of 9.1% in 2004-2005, and have more recently decreased slightly to 8.7% in 2010[5].

Although direct causality cannot be established for preterm birth, there are multiple risk factors which influence preterm birth rates. Some of the largest contributors to the rising trend are believed to be assisted reproductive technologies, multiples births and obstetric interventions such as induced labours and Caesarean sections[52]. In Canada alone multiple births are accelerating, with an incidence rate increase of 18% from 1993 to 2002; this becomes even more significant given the birth rate has dropped 19% over that same period[42].

Prematurity is associated with a higher risk of adverse health consequences; this highlights the importance of research into prematurity, especially considering it is the leading cause of newborn deaths in infants, and is second only to pneumonia in children under five[52,58]. Furthermore, despite preterm birth being a major risk factor for morbidity and mortality, it also has a large burden on health, education and social services throughout the infant's childhood[27]. Costing studies have shown that health care costs are inversely correlated with infant's GA, and there is extreme variability of costs within each GA group[52, 53]. One literature review found hospital costs have been seen to be as low as $4500 (US) for late prematurity, and as high as >$100,000 for extremely preterm infants[52].

1.1.1 Very Preterm Infants

The population of interest in this study is very preterm infants (VPI). For the purpose of this study, VPIs are defined as infants that have either a very low birth weight (VLBW), <1500g, or a very low gestational age (VLGA), <32 weeks[46]. In developed countries very preterm infants account for only about

1% of births but 40-60% of all infant and perinatal mortality[18]. VPIs require extensive healthcare services during their first year of life, and the cost increases with every decrease in GA at birth[30, 53]. There is a wide range of resource utilization within very preterm infants, where extremely preterm infants (<28 weeks) have almost 6 times higher costs and hospital lengths of stay (LOS) than late preterm infants (32-36 weeks)[23]. This difference is due to the complex maturation pace of all infants, influenced by GA at birth, birth weight, spontaneous labour, premature rupture of membranes and varying degrees of neonatal illness[6, 7].

1.2 Health Technology

Subspecialty perinatal centers such as neonatal intensive care units (NICU), are fundamental to very preterm infants through their highly-specialized and timely healthcare services[9]. NICUs have evolved rapidly over the last few decades and their utilization has led to drastic reductions in mortality and morbidity of newborns; this is in part due to the introduction of treatments such as surfactant, antenatal corticosteroids and changes in respiratory management[28]. Given the NICU's importance, one of the key challenges in healthcare management is ensuring equitable care, as NICU beds fill quickly and stay filled given a preterm infant's long length of initial hospital stay[11].

1.3 Alberta's Current Health Landscape

Healthcare in Alberta operates as a centralized organization with one provincial system. Alberta Health (AH) sets, monitors and enforces health policy while managing capital planning, and outcome measures; Alberta Health Services (AHS) oversees the planning and delivery of health services to all Albertans[2]. Integrated within AHS is the Alberta Perinatal Health Program (APHP), which works with key stakeholders to achieve and promote optimal perinatal practise[4].

In 2004 AH divided Alberta into nine geographical zones which are called health zones, these regions were later abolished in 2008 and replaced with five zones, and they include: South, Calgary, Central, Edmonton and North. Edmonton and Calgary health zones contain the majority of the province's population (2.6 vs. 1.2 million in 2008) and have a far greater population density when compared to the other zones[2].

1.3.1 NICU Centralization

In Alberta, specialized tertiary NICUs designed to treat high-risk groups, such as VPI, are centralized within Calgary and Edmonton. Currently there are two tertiary NICUs in each city, and other health zones do not have these high level dedicated NICUs. Zones with lower level NICUs must instead have referral systems that require physicians to identify high-risk pregnancies early on, and ensure deliveries occur within the proper hospital with the appropriate level of neonatal care. Current research monitoring regionalized perinatal programs are finding regionalization is correlated with improved perinatal outcomes[45]. The ideal regionalized system is one that distributes medical services across a region, in such a way that it ensures all levels of health services are accessible to the entire population while remaining cost-effective. This study considers the Albertan neonatal care system to be "centralized" as multiple tertiary NICUs are located in the same city center, which may limit accessibility in other health zones. It should be mentioned this stance is debateable, as proponents of self-identifying as regionalized would state the Albertan neonatal care has a Northern and Southern Albertan Neonatal Program (NANP, SANP), where each program is centered around Edmonton or Calgary and attempts to provide medical services equitably across its territory.

1.4 Objectives

The objectives of this study are:

1. To compare and test VPI health outcomes (mortality) and service utilization (LOS, NICU admission, transfers) across Alberta health zones
2. To investigate the impact of distance from VPI's home to nearest level 3 NICU center has on health outcomes.
3. To explore current and alternative NICU allocations in Alberta, taking into consideration travel distances for all VPI, and to provide recommendations for the most equitable allocation.
4. To quantify and test VPI inpatient costs overall and by health zones in Alberta

1.5 Significance

Given the rising rate of preterm births and its associated impact on health outcomes and resources utilization, this study holds great importance. Currently there are few Canadian costing and health outcomes studies evaluating VPI, and even fewer studies based on Alberta data. In order to justify our current resource allocation it is important to have Alberta-specific results on the program's costs, effectiveness and impact on health equity[52]. Inter-provincial benchmarking would be optimal, but an inter-regional analysis is the first step in identifying opportunities for improvement.

Since Alberta has a centralized health system with one administrative entity, it has the ability to quickly implement a system-wide approach. This means research evaluating NICU equity and effectiveness of care between regions could potentially lead to future strategic health service changes if large disparities exist within the system. As echoed by researchers and practitioners, the impact of NICU resources have yet to be well described in Canada, and there is a need for detailed breakdowns of resource usage among preterm infants[11].

2 LITERATURE REVIEW

This chapter provides a summary of the scientific literature on preterm infants in the following key areas: NICU services, healthcare access, health outcomes/utilization and costing; each area is also covered in one of the paper's objectives. The literature review used MEDLINE as the major electronic bibliographic database, and restricted the search to articles written within the last fifteen years in English and with a population of interest from developed countries. The population of interest was preterm infants (with a focus on VLBW and VLGA infants), and other key search parameters used to address the objectives included: regionalization, hospital costs, length of stay, mortality, service usage, centralization, neonatal intensive care unit (NICU), and healthcare access.

2.1 Background - Canadian Neonatal Care

In Canada neonatal care has rapidly evolved in complexity over the last few decades, which has resulted in improvements in health outcomes. Perinatal care in NICUs is the main driver in reducing mortality and morbidity in preterm infants, due to technological advancements such as surfactant and antenatal corticosteroids use[51]. A comparison using the Canadian Neonatal Network of NICUs across late preterm (34-36 weeks) and early term infants found length of stay and need for respiratory support decreased with increasing gestational age[11]. It also found late preterm infants have the greatest impact on NICU bed occupancy, as a large proportion of this group are being admitted because they are at risk for key morbidities. When comparing late preterm to term infants the need for specialized NICU care is clear, children born late preterm are at a higher risk of complications such as respiratory distress, intraventricular hemorrhage, and cerebral palsy; furthermore the mortality rates are three times higher[11]. Another diagnostic tool to evaluate the high risk newborn group is birth weight percentiles given gestational age. One Canadian study found small for gestational age (SGA) infants (below the 10'th percentile for weight given age) who are singleton and very preterm (<32 weeks) have a higher odds of mortality (OR 2.46), prolonged stays in NICU care, and an overall higher resource utilization compared to non-SGA very preterm infants[43].

In Canada multiple births have accelerated from 1993 to 2002 by 18%, despite a decrease in the birth rate by 19%[42]. Multi-births are strongly correlated to VLBW status, and this shift has a key role in the rise of preterm births in Canada. In Alberta, preterm birth rates have risen to 8.4 per 100 live births in 2007, which is reflected by the rise in multiple birth rates to 3.4 per 100 live births (SGA rates to 8.2 per 100 births)[5]. The increase in preterm births are linked to a variety of key factors, such as an increasing rate of induction of labour and higher utilization of artificial reproductive therapies [28]. These dynamics also affect Alberta's neonatal mortality rate and service utilization. Peters et al., (2009) reported that between 1999 and 2004 the neonatal mortality rate was 8.3%, and healthcare utilization in a sample of VLBW infants in Edmonton followed for 18 months since birth had a median hospital lengths of stay of 84 days[39].

International comparisons on Canada's ability to perform advanced neonatal care could allow for benchmarking and finding opportunities for improvement. Unfortunately the literature on international comparisons is sparse for Canadian VLBW/VLGA infant populations, and this paper only found a 2012 study comparing VLBW infants in Canada and Japan. The Canadian sample obtained infants within the Canadian Neonatal Network, which records all infants admitted to a tertiary NICU in Canada. It found Japanese VLBW infants admitted to NICUs had a mortality rate odds ratio of 0.87. Canada also had higher rates of maternal hypertension, outborn births (non-NICU) (19.1% vs. 7.6%) and multiple births[25]. Mortality rates are summarized in Table 1 by gestational age, but the overall mortality rate for all VLBW in Canada was 10.5% compared to 6.5 % in Japan.

Table 2.1: Mortality rates for VLBW infants admitted to NICUs from 2006-2008[25]

	<25 weeks	**25-26 weeks**	**27-28 weeks**	**29-32 weeks**	**>32 weeks**
Canadian Mortality	52.3%	17.9%	7.3%	1.7%	1.4%
Japanese Mortality	27.1%	9.6%	4.1%	1.4%	0.5%

Source: Isayama, et al., 2012

2.2 Key Healthcare Services - NICU Care

The introduction of neonatal intensive care units has improved outcomes of high risk infants born preterm or with serious medical conditions[8]. A complex system involving levels of NICU care was established to help specialize services, and meet the widely different needs of the newborn population (see Appendix 7.2)[17]. Scientific journal articles on NICU admittance rates and differences in health outcomes by level of care (primary, secondary, and tertiary) received, are important in pushing for healthcare improvement and benchmarking neonatal services across countries and regions. An Italian study on VLGA infants found the probability of fetal mortality and not being in a level 3 facility (tertiary) was associated with a lower education level of the mother, not having pregnancy complications, or living outside a metropolitan area[18]. In 2003 the Cincinnati region had an 88.2% birth rate in level 3 NICU centers for VPIs. They also determined the odds of death or morbidity in VPI was 3 times higher in nontertiary centers compared to subspecialty perinatal centers[12]. These results were slightly higher than a study in the same region following a VLBW infant cohort in 1997, which found infants born at a non-subspecialty center had an increased odds of death of 2.64[56]. The same results were found in Finland and England, where a level 3 facility when compared to a lower level, reduces the odds of mortality[47, 57]. Another key trait shown to increase mortality was if a VPI was not born during office hours[47].

NICU volume has been seen as an important factor in determining and improving high risk neonate survival. The American Academy of Pediatrics has found NICUs treating less than 100 patients per year had an odds ratio for death of 1.78 when compared to NICU treating more than 100 patients per year[8]. However critics have argued the indicator is debateable, as volume only explains 9% of the variation of mortality rates, while other hospital characteristics explain another 7%[44]. When comparing hospitals with low levels of care and low volumes (<100 patients per year), to hospitals with high levels of care and high volumes, a California study determined the lower facility had a higher mortality risk as seen in their odds ratio confidence interval of 1.19-2.70[40]. Lower volume cut-offs of 50 VLBW admissions per year has been studied in Vermont, and they found hospitals with less than the cut-off would have an 11% reduction in mortality with an additional 10 admissions per year[44]. Currently, volume alone is not identified as a key indicator in the literature, as it only explains a small proportion of the measured variability between neonatal centres (positive predictive value of 9%)[26]. Although a cut-off has not been established, some specialists believe a base requirement of at least 10 VLBW neonates per year should be the lowest number allowable by a unit, in order to ensure the facility is adequately experienced [26].

2.3 Healthcare Access

2.3.1 Regionalization of Neonatal Care

Regionalization of perinatal health services is the "rational distribution of medical services across a geographic area, ensuring services and facilities at all three levels (primary, secondary and tertiary) are located in such a way as to offer both easy access to the population and cost-effective care"[45]. The most effective high risk neonatal regionalized systems incorporate both maternity and neonatal care. The systems must identify early signs and symptoms of high risk pregnancies, as it is fundamental to ensure a good referral system is in place, so all mothers deliver their newborns at the appropriate facility[45].

In 1976 the Committee on Perinatal Health and the March of Dimes organized a model for the regionalization of perinatal services across the US with three distinct specialty levels[36]. This system was later credited with providing cost-effective care while reducing neonatal mortality. Despite this, deregionalization began to occur after 1993 and there was an increase in high risk preterm infants being born outside level 3 facilities. New guidelines arose in 2004 from the American Academy of Pediatrics that continued to stress the importance of level 3 facilities for very preterm infants, and since then progress has slowly moved towards the goal of having 90% of all VLBW infants being born in a level 3 center[33]. Despite regionalization's ability to improve utilization of resources and outcomes, neonatal care requires some centralization of specialized services. A regionalized approach that blankets an entire patient population through excessive level 3 facility construction, will result in an inadequate yearly volume of high risk patients reaching these facilities. Adequate patient volume is key to ensuring efficiency, acute patient experience and high healthcare quality[32].

Literature on perinatal regionalization has found that it is related to improvements in perinatal health outcomes. Regionalization seeks to optimize access to care, allowing for a theoretical improvement in tertiary NICU admissions. In extremely premature infants, tertiary care greatly improves both neonatal mortality and morbidity[24]. Both a Canadian and US study had very similar results in very low gestational age infants (<32 weeks); they found outborn infants (born outside a level 3 facility) were at a greater risk of death (OR=1.62-1.70)[16, 34]. They also found outborn infants were at a higher risk of complications, such as intraventricular hemorrhage, respiratory distress syndrome and nosocomial infection[16]. Regionalization has also been seen as a tool to address the United Nation's Millennium Development Goals, of a reduction in child mortality by two thirds before 2015. Since 40-50% of all child mortality is early in/right after the neonatal period, an effective regionalized system would improve both maternal and neonatal outcomes[45].

2.3.2 Distance to Neonatal Services

Specialist services are more commonly being organized on a regionalized basis, and clinical resources and experts are concentrated in areas of higher populations[56]. In the United States 83.5% of level 3 NICUs are located in metropolitan areas, and the longest maternal ground transport time to one of these facilities is from rural areas[13]. Geographic barriers to health services can adversely impact health outcomes, and policy makers need to ensure facility planning and hospital network creation address these limitations and maximize clinical benefits[19]. These issues have pushed health systems into adopting a regionalized system, which can improve upon patient's clinical outcomes if distance and time are impediments to healthcare access[56]. Unfortunately, while converting to a regionalized system, facilities may be allocated across a health network based on political influence or guesswork, as decision makers usually lack an objective methodological framework[19].

There is a need for a more objective decision making tool, such as advanced geographic information system (GIS) models that can plan these health networks and account for data on travel time, costs, and health outcomes. GIS mapping allows providers and policy makers to visually analyze and understand how current and future hospitals can adequately cover a patient population's health service needs. Level 3 facility construction and allocation should not be strictly based on supply and demand, but costs (long distance travel, transfers, family's lost wage while visiting) and ease of access to a population is another critical factor[13].

2.4 Health Outcomes and Service Utilization

2.4.1 Mortality & Length of Stay

Health outcome measures like survival rates and length of stay are so important due to their wide range of uses, from counseling parents, to informing care and clinical pathways, to even a higher macro level of service planning and delivery[35]. Despite one Swiss study stating the VPI birth rate slightly increased from 1996 (0.87%) to 2008 (1.10%), during this same period survival free from major complications increased from 66.9% to 71.7%[48]. These complications (bronchopulmonary dysplasia, intraventricular hemorrhage) may have been mitigated due to a 20% increase in antenatal corticosteroids and surfactant use over the same 8 year period; and other strategies such as a decreased use of supplemental oxygen and stronger lung-protective ventilation strategies[48].

Although organizational measures are being used to improve health outcomes, such as regionalization and the creation of neonatal care hospital networks, there are considerable variations in healthcare service usage and health outcomes both within and between countries[37]. Table 2.2 shows results from the European Health Care Outcomes, Performance and Efficiency group (EuroHOPE), a comparison of very preterm infant's health outcomes across seven European countries. It determined that one year mortality was lowest in Nordic countries and Scotland, and highest in Hungary, Italy and the Netherlands[37]. An article following a Finnish VPI population found the overall survival was 87%, with a mean length of stay of 53 days. However, there were large differences in the length of stay between different hospital districts (up to 10 days)[29]. The same variation by hospital district was also seen in the proportion of VPI born in a level 3 NICU facility, which ranged from 53% to 94%. One of the highest survival rates observed in the literature was from a UK study on VPI admitted to a NICU. 91.9% of all singleton infants born at 23 to 32 weeks gestational age survived to discharge, and when stratified by gestational age, at 25 weeks GA the survival rate was 73% for males and 67% for females[35].

Table 2.2: Health Outcomes of VPI across multiple countries[37]

	Finland	Hungary	Italy	Netherlands	Scotland	*Sweden (linkable)	*Norway (linkable)
1 year mortality rate	12.9%	18.1%	13.8%	13.1%	6.3%	8.0 %	5.5%
Average Hosp. Ep. LoS (days)	47.1	46.0	59.1	31.7	35.2	65.7	32.2

Source: Numerato et al., 2015
*****Follow-up treatment for one year was only available for ~60% of infants, which caused a bias that downwardly skewed mortality rates*

2.4.2 Transfers

Since NICU treatment is required for every very premature infant, a health system has to ensure these infants are being treated at a tertiary care center. It has been shown those infants born in a level 3 facility have significantly better health outcomes when compared to those born at a level 2 or lower level hospitals. One study from Hawaii attempted to look at survival rates for extremely preterm infants transported to a level 3 compared to those born at a level 3 facility. They found survival rates were identical, but the transport group had significantly longer lengths of stay and higher rates of complications, such as severe retinopathy of prematurity when compared to the inborn group[32]. Another study from the Canadian Neonatal Network also reported similar results of higher complications in transported individuals, but both inborn and outborn infants born at 25 weeks GA had similar rates of survival[15]. This evidence highlights the importance of early screening and ensuring that high risk mothers are able to deliver at a hospital equipped to service their required level of care.

Despite the importance of seeking tertiary care for premature infants, long hospitalizations could also have a negative impact on infants and their families. Prolonged hospitalizations expose infants to adverse environments, opportunistic viruses, and impede early parent-infant relationship building[29]. Back transfers to a lower level unit before discharge can improve the efficiency of bed utilization in level 3 NICUs, bring an infant closer to home, and result in cost saving due to a less expensive daily bed cost at a lower level unit[29]. This back transfer technique must also be weighed against competing evidence, that compared back transferred infants to those who stayed in a level 3 facility. The back transfer group had an increased odds of retinal disorders (2.43 OR) and asthma (1.31 OR), but fewer viral infections (0.75 OR)[46].

2.5 Economic Costing

With the rise in preterm births, economic literature has explored the short term implications of preterm births on the health systems/hospitals budget and resource usage. Although a societal perspective may be ideal for economic analyses of preterm births, all research in this area approaches the issue from a healthcare service perspective. A healthcare service perspective looks at all costs directly attributable to the organisation, while a societal perspective is ideal since it accounts for more than just hospital expenses, but also the economic impact on the welfare of an entire society, such as the long-term health issues and the required future educational assistance for developmentally delayed children[22].

Literature on the long term cost implications of very preterm infants has found that the initial hospital stay comprises 79.5% of the total 4 year hospital costs[30]. This is critical as this study's population has a year of follow-up, so all cost estimates during our study period will comprise at least 80% of the total 4 year hospitals costs for these infants. This finding of high resource intensity within the first year, is further reinforced by a Canadian study following VPI over 10 years. It found the average in-hospital length of stay in the infant's second year was only 1.6 days[27]. This evidence helps for understanding the distribution of costs over time, as a longer study duration will show a lower cost per QALY or increased cost-effectiveness. This cost per QALY has been estimated in a Finnish study of very preterm infants from 2000-2003. They determined the average cost per quality adjusted life year (QALY) over four years was $28,290/QALY (2008 US Currency) for VPI compared to the average child at $1,636/QALY[30].

Key drivers of costs become complicated in very preterm infants due to diagnoses being strongly correlated to maternal risk factors or complications. Complications such as bronchopulmonary dysplasia, necrotizing enterocolitis, intraventricular hemorrhage, and retinopathy of prematurity were identified as major cost drivers in the literature[30]. Other cost drivers classified under non-personnel costs for extremely premature infants included procedures such as: surfactant usage, red blood cell transfusions, chest radiograph, cranial ultrasound, abdominal radiographs, echocardiogram usage, parenteral amino acid infusion, platelet transfusion, and surgery. Overall these procedures explained 91% of variability in daily non-personnel costs in NICUs across Canada[60].

Costing studies have taken different approaches in evaluating preterm infants, either by gestational age categories or birth weight. Gestational age has been found to be a better predictor for costs as hospital costs decrease exponentially with advancing age, however, birth weight still provides valuable information to decision makers[20]. The results of a California study on singleton deliveries 25-38 weeks GA and weighing between 500-3000g can be seen in Table 2.3. Using either birth weight or gestational age, the extremely premature infant population can be seen having costs exceeding $200,000. This information is extremely valuable to clinicians, policy makers and health researchers within the population's country of origin. The difficulty is in transferring results to a specific country or context, because health systems differ, from basic cost calculations to population demographics, and even clinical procedures/guidelines[52]. However, these country specific measures allow for international benchmarking, comparing the economic burden of a health system through measures such as cost per patient, or service utilization.

Table 2.3: Hospital cost of singleton deliveries by specific gestational week and weight category in California[20]

Grouping	Average Cost*
25 weeks GA	$ 202,700
26-27 weeks GA	$ 133,250
28-29 weeks GA	$ 74,400
30-32 weeks GA	$ 38,100
33-35 weeks GA	$ 7,460
36-38 weeks GA	$ 1,800
500-700 g	$ 224,400
750-999 g	$ 144,000
1500-1749 g	$ 33,400
2250-2500 g	$ 4,300
>3000 g	$ 1,000

Source: Gilbert et al., 2003
**All costs in 2002 US dollars*

Benchmarking between Canada and the United States shows similarities in costing between the two countries despite differing health systems and service delivery. In the United States preterm and low birth weight infants represented 9% of all births, but 47% of all infant hospital costs and 27% of all pediatric stays[50]. In both Canada and the United States extremely low gestational age infants (<28 weeks and <1000g) shared similar costs, where the US averaged US$65,600 (2001) per infants and Canada CAN$67,467 (2012)[28, 51]. When comparing the extremely premature to preterm (28-32 weeks) infants, costs were on average four times higher[51]. A national budget impact analysis in Canada estimated early, moderate and late preterm costs to the health care system at $123.3, $255.6 and $208.2 million respectively[27]. The US, given its larger population, had a higher overall yearly cost, but the budget impact analysis followed the same pattern, and the largest proportion of the budget was observed in the moderately preterm (28-32 weeks)/low birth weight infants, due to the high treatment costs and the large number of cases per year[51].

3 METHODS

3.1 Dataset Creation

The study population consisted of very preterm infants born from April 1 2004, to March 31 2009 in Alberta. This study population is a sub-population of low birth weight infants (<2501g) born over the same period. All births are live-born, and are registered within the Alberta Perinatal Health Program (APHP). The APHP is integrated within Alberta Health Services and provides a comprehensive listing of clinical data from birth to the first year of life[4].

In order to expand the surveillance period of each infant and obtain further clinical records, the APHP database was merged to the Vital Statistics Death Registry, Population Registry, Postal Code Database, CIHI Costing Database and the Inpatient File (Discharge Abstract) Database[3]. This created a dataset with at least a year of follow-up data for each patient. The merge procedure was accomplished using each infant's unique healthcare number (ID). To ensure ethical considerations were accounted for, each healthcare ID was anonymized to maintain patient confidentiality. The dataset contains information on the following: date and cause of death, all inpatient hospital records from birth to study end, distances from patient's home address to NICU facilities, costing estimates and indicators of out-migration for any individual within the study (for a full list of variables see Appendix 7.3).

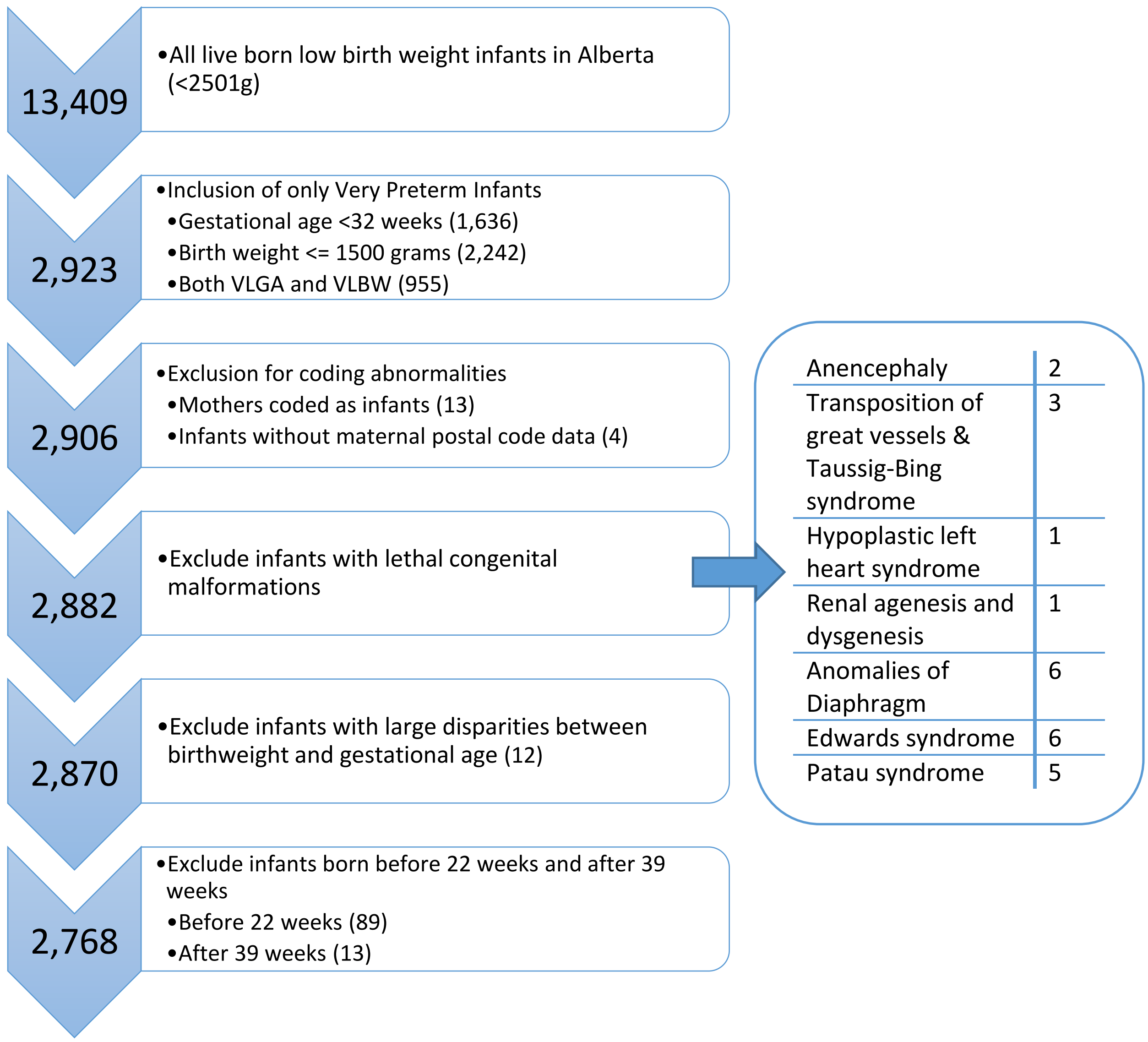
Table 3.1: List of databases merged to form the study's dataset[3]

Database	Description
Alberta Perinatal Health Program (APHP)	Perinatal data from the provincial delivery record for all hospital births and registered midwife attended home births in Alberta. The data was collected to optimize infant and maternal outcomes and support studies of perinatal mortality.
CIHI Costing Database	Data for each hospital in Alberta and its "Cost of a standard hospital stay" or cost per weighted case (CPWC).
Discharge Abstract Database (DAD)	CIHI standardized data that provides administrative, clinical and demographic information on hospital discharges (deaths, sign-outs and transfers). This data is directly from acute care facilities or the regional health authority.
Population Registry	An Alberta Health registry containing basic demographic, socioeconomic and social services data
Postal Code Database	An Alberta dataset containing all Alberta postal codes and corresponding geographic coordinates
Vital Statistics Death Registry	Morality data for Alberta listing cause and time of death

3.2 Inclusion/Exclusion Criteria

To be included in the study, all LBW infants from the original population had to be either VLBW (weight at birth less than or equal to 1500 grams) or VLGA (gestational age (GA) at birth before 32 weeks, see Figure 3.1). Infants with incomplete ID's or an ID that could not be linked back to our merged provincial databases were excluded. Infants born before 22 weeks of GA and after 39 weeks of GA were also excluded, as were infants with major disparities between GA and weight[37, 34]. Infants with the following congenital malformations were excluded: anencephaly, transposition of great vessels, hypoplastic left heart syndrome, renal agenesis and dysgenesis, anomalies of diaphragm, Patau syndrome and Edwards syndrome (see Appendix 7.1)[37] These exclusions are consistent with those used by the EuroHOPE group and closely resemble the Performance, Effectiveness, and Cost of Treatment Episodes (PERFECT) Preterm Infant Study Group in Finland. Aligning the study methodology with these studies allows for international comparisons. After all exclusions there were a total of 2,768 Albertan infants included in the study, born between the years 2004-2009.

Figure 3.1: Inclusion/Exclusion Procedure



3.3 Variables of Interest

The study included the following variables of interest: Gestational age at delivery (weeks), gender, infant born a singleton or multiple birth, Apgar score at 1, 5 and 10 minutes[49], hospital length of stay, small or large or normal (appropriate) for gestational age, any non-lethal malformations, hospital NICU capability and/or level, whether infants were transferred to a level three NICU capable hospital, Albertan health zone/region, gestational age at delivery (weeks), driving distance to a NICU, cost of hospital stay, teaching hospital status, mortality, and various other maternal risk factors.

Hospital NICU levels according to both the literature and Alberta Health, consist of three groups ranging from level 1 to 3. Appendix 7.2 outlines each level in detail, but in summary, level three provides the highest level of neonatal care through advanced imaging and specialized clinicians to treat high risk neonates[8]. Transfers accounts for infants admitted into one hospital but are later discharged and admitted to another hospital. This study defined it as those patients discharged and admitted within a day to different hospitals (or the same hospital in different wards). Our variable for transfers accounts for administrative database discrepancies, where a transfer also occurs if they are admitted a day before discharge or a day after discharge. Variables accounting for transfers to and from a level three hospital were created to better understand if the current NICU system in Alberta (see Figure 3.2) has an effect on transfers rates and infant health outcomes.

Hospital length of stay (LOS) was calculated in two distinct ways, the first being the length of stay from hospital admission to discharge, while hospital episode length of stay (HEPLOS) contained all continuous hospital stays (including transfers), from birth to discharge. LOS is coded in days and is derived from the Discharge Abstract Database's (DAD) coding of date of hospital admission and discharge.

The variables small/large/normal for gestational age is a critical indicator created using the Canadian Perinatal Surveillance System (CPSS) cut-offs, as recommended by the Public Health Agency of Canada (PHAC)[31]. Although VPI has a distinct definition of infants being VLBW or VLGA, the birth weight size given their gestational age allows for further stratification, where a VLBW infants could be large for their gestational age if their birth weight is in the 90th percentile or higher of infants at their gestational age.

The study excluded infants with key lethal malformations in order to limit bias when interpreting mortality rates across groups of the study population. Non-lethal malformations were accounted for as they could impact overall health and may be associated with morbidity and mortality in the infants. These were identified as ICD-10 codes "Q00-Q99" (Congenital malformations, deformations and chromosomal abnormalities) in the DAD.

Hospital costs were calculated through resource intensity weights (RIW) found in the DAD, and the average cost per standard hospital stay in the CIHI costing database[14]. The resulting cost calculation is an estimate (excluding physician payments and amortization expenses on land/building equipment), and so all the strengths and limitations of a costing estimate must be taken into account when interpreting results based on this methodology compared to direct cost measurement.

Every maternal postal code was mapped through graphical information system (GIS) software to calculate distances to the nearest NICU facility. These distances follow roadways and were calculated as the shortest distance between the two points.

3.4 Statistical Analysis

3.4.1 Infant Outcomes

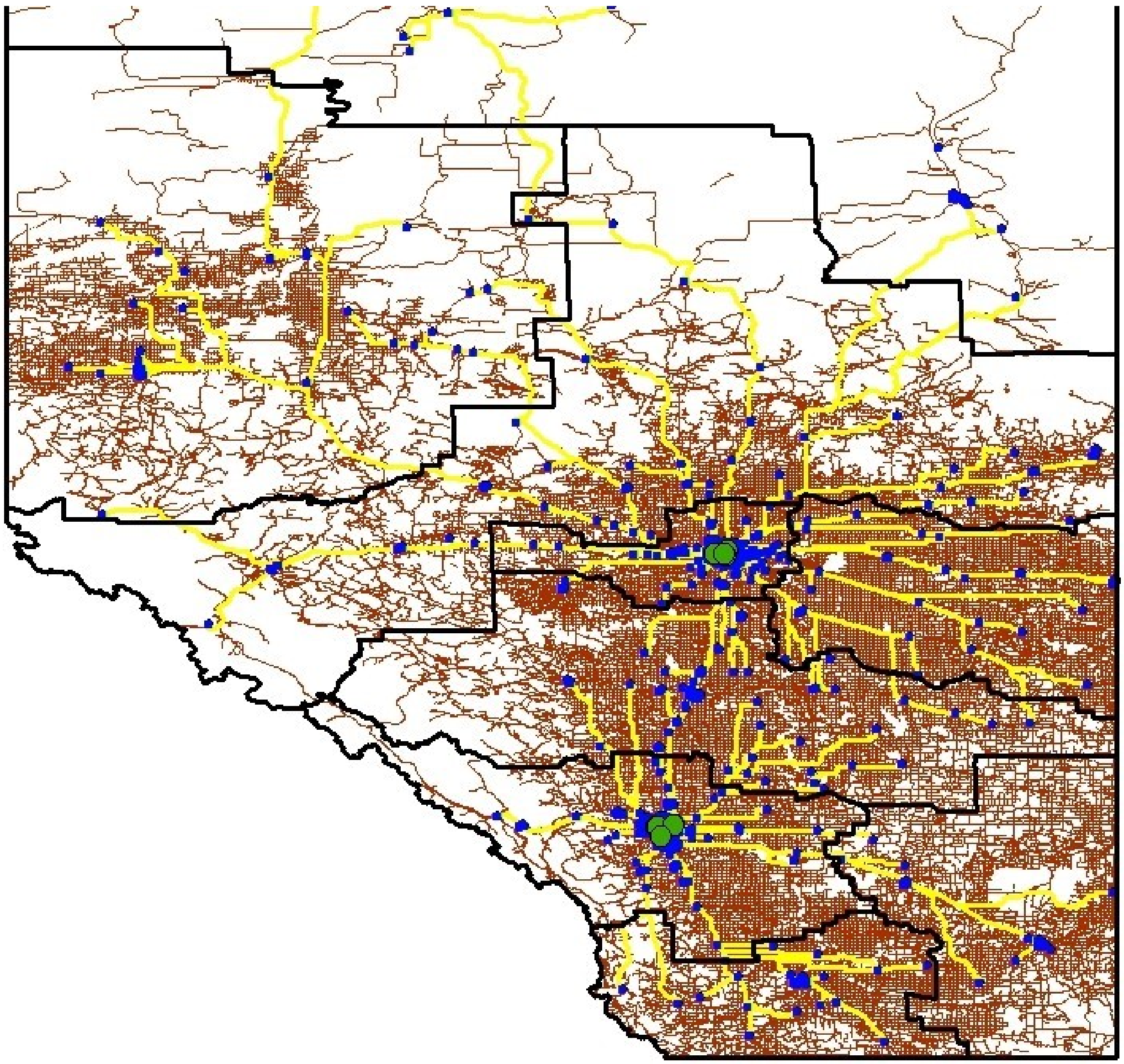
Demographic variables were tabulated, and regression analyses were conducted on mortality (30 days, 1 year), hospital episode length of stay and total length of stay within a year. Analyses followed the PERFECT project methodology, where a logistic regression was performed for mortality, and a negative binomial regression for length of stay[21, 40]. A logit model is a nonlinear regression model used when the dependent variable is binary. It estimates the probability on a 0-1 scale, with 0 indicating no death and 1 indicating death. A negative binomial regression is used for over-dispersed count data such as LOS, and it provides a narrower confidence interval when compared to a Poisson regression model[21]. In order to test the model's fit, a covariance matrix of the coefficients was run to determine correlation between the coefficients. The outcome measures were risk adjusted for health zone/region, level three NICU hospital admission, gestational age, Apgar score, size for gestational age, transfers, multiple births, mother's first delivery, non-lethal malformations, and whether they were living in the city with a level three NICU facility (Calgary/Edmonton).

3.4.2 Distance Calculation and GIS Modeling

Distance was calculated in both kilometers and meters, and required the use of the Albertan postal code database, along with ARCMap (GIS software) [10]. ArcMap is the main program in ArcGIS, a geospatial processing program used to analyze and create geographic data and interactive maps[10]. Maternal postal codes were merged with the postal code database to obtain the latitude and longitude of each home address. These longitudes and latitudes were then exported into ARC Maps and placed on a road network of Alberta, obtained from the Government of Canada's open source database[57]. Once each VPI's house was plotted on the map, all level 2 (Special care nursery) and 3 (NICU) hospitals were also placed on the road network using latitudes and longitudes of their address (see Appendix 7.4). Distances from each house to each NICU capable hospital was calculated using the Origin Destination (OD) Cost Matrix function in ARC Maps. Distance from the infant's home address to NICU was chosen over distance from nearest emergency room (ER) to NICU because of the high usage of screening in the VPI population. Therefore it would be extremely uncommon to have a mother arriving at an ER, as the overwhelming majority would be admitted to a hospital equipped with NICU services prior to their delivery. Once all distances were calculated, the data was exported and merged into the VPI dataset through unique identifiers.

Two location-allocation methods were used in ARC Maps to statistically optimize the allocative efficiency of NICU facilities in Alberta. Therefore the models attempted to theoretically optimize the distance from the patient's home to a NICU based on different factors. One model minimized the weighted impedance, which meant it optimized the demand allocated to a facility, multiplied by the impedance (time to facility multiplied by distance) to the facility. The other modelling strategy was to maximize capacitated coverage, this model mimicked the first model while also accounting for the finite capacity of NICU facilities. The maximum capacity of NICU's were calculated using the average NICU LOS in VPI and the available number of beds in each facility. The model conservatively assumed 80% of all NICU LOS usage is consumed by VPI, and the NICUs were running on average at 90% capacity/efficiency. For both models level 2 and 3 facilities were used for potential NICU locations. These hospitals were used because of their pre-established neonatal care practices/equipment, and the simpler upgrade that would be needed to convert a level 2 facility to a level 3 facility (relative to a non-neonatal hospital).

Figure 3.2: GIS Mapping of Maternal Postal Codes and Routes to Nearest NICU Facility



**Note: Yellow lines represent driving routes to the nearest level 3 NICU facility (green circle). Blue circles represent VPI home address and brown lines represent road networks.*

3.4.3 Costing

Hospital costs were calculated with the Canadian Institute for Health Information's resource intensity weight (RIW) values and the annual average standard cost of a standard hospital stay. As standard cost per hospital stay (SCHS) is a hospital specific estimate, for those hospitals without a SCHS a health zone average was used. Each SCHS is year specific, so it is matched to the year of patient hospital admission. The RIW and SCHS are multiplied together to create a weighted cost estimate for each admission. For costing relationships and the budget impact analysis, costs were summed for each hospital stay, infant, health zone, and for a categorical classification of distance to a level 3 NICU facility. To note, all costs were estimated using the 2010-11 cost per standard hospital stay, which means all cost estimates are in 2010 Canadian dollars.

Costing data was also fundamental to evaluating the allocative efficiency of the current NICU distribution. In order to justify the need for a re-allocation of the NICU facilities, the data needed to indicate distance led to sub-optimal health outcomes, reduced access to services, or higher resource utilization. For resource utilization (costs), a generalized linear regression (GLM) was used due to the costing data being positively skewed[38]. The GLM was run using a gamma distribution and a log link to account for the non-normally distributed data. The goal was to understand if distance was a significant indicator for total cost and the magnitude and direction of that relationship.

4 Results

4.1 Summary Statistics

There were 2,768 VPI in the study following application of our inclusion and exclusion criteria. Over the study period the yearly birth rate average for VPI was 1.57% of all live births in Alberta from 2004 to 2009. The highest rate of VPI births (1.72% of all live births) occurred in 2005-2006. For reference, the preterm birth rate from 2004-2009 in Alberta was 9.12% of all live births.

Table 4.1 shows the breakdown of VLBW or VLGA infants for each health region. Around 34% of all VPI were labelled as both VLBW and VLGA, although a greater proportion of the overall study population are VLBW. Overall these rates are consistent across each health region, with the only exception being Edmonton and Calgary VLBW, who are about 2% higher and lower, respectively, than the provincial average.

Table 4.1: Very Preterm Infant breakdown by VLBW & VLGA status (2004 – 2009)

	Alberta	Calgary	Central	Edmonton	North	South
Very low birth weight babies, N (%)	2092 (75.6)	813 (76.6)	241 (76.5)	675 (73.5)	260 (76.2)	103 (77.4)
Very low gestational age babies, N (%)	1624 (58.7)	593 (55.9)	184 (58.4)	565 (61.5)	203 (59.5)	79 (59.4)
Both VLBW & VLGA, N (%)	948 (34.2)	345 (32.5)	110 (34.9)	322 (35.1)	122 (35.8)	49 (36.8)
Avg. VPI % of Total Yearly Birth Rate	1.57	1.34	1.61	1.46	1.76	2.08
Avg. Preterm % of Total Yearly Birth Rate	9.12	9.22	9.44	9.12	8.80	7.56

Table 4.2 shows a detailed breakdown of gestational age (GA) and birth weight (BW) for each health zone. The sample size within each region follows population dispersion across the province, where Calgary and Edmonton hold the majority of the provinces population. The distribution of GA and BW groups across health regions appear balanced. However, the percent of <25 weeks GA is highest in Calgary at 11%, which exceeds the Albertan average (9.4%). This is a key group that strongly affects overall mortality and likely explains the higher rate of infants with a BW <500g (3.2%). Another way of framing the difference and its magnitude is by stating Calgary has roughly 50% of all VPI born at the lowest GA and BW.

Table 4.2: Very Preterm Infant's Gestational Age and Birth Weight Breakdown by Health Zone

	Alberta	Calgary	Central	Edmonton	North	South
	N (%) infants by GA - weeks					
22-24	261 (9.4)	117 (11.0)	23 (7.3)	79 (8.6)	32 (9.4)	10 (7.5)
25-26	355 (12.8)	122 (11.5)	40 (12.7)	125 (13.6)	50 (14.7)	18 (13.5)
27-28	467 (16.9)	172 (16.2)	52 (16.5)	154 (16.8)	68 (19.9)	21 (15.8)
29-30	772 (27.9)	282 (26.6)	96 (30.5)	269 (29.3)	85 (24.9)	40 (30.1)
31-32	724 (26.2)	278 (26.2)	79 (25.1)	242 (26.4)	90 (26.4)	35 (26.3)
>32	189 (6.8)	90 (8.5)	25 (7.9)	49 (5.3)	16 (4.7)	10 (6.8)
	N (%) infants by birth weight					
<500	61 (2.2)	34 (3.2)	3 (1.0)	19 (2.1)	5 (1.5)	0 (0.0)
500-749	316 (11.4)	131 (12.4)	33 (10.5)	91 (9.9)	43 (12.6)	18 (13.5)
750-999	460 (16.6)	180 (17.0)	46 (14.6)	156 (17.0)	47 (13.8)	31 (23.3)
1000-1249	502 (18.1)	178 (16.8)	71 (22.5)	173 (18.9)	57 (16.7)	23 (17.3)
1250-1499	727 (26.3)	282 (26.6)	84 (26.7)	226 (24.6)	105 (30.8)	30 (22.6)
>1499	702 (25.4)	256 (24.1)	78 (24.8)	253 (27.6)	84 (24.6)	31 (23.3)

Table 4.3 provides basic demographic measures by health zone, and tests whether the mean value or proportion is significantly different from the provincial average. The South zone had the lowest average birth weight (1188g), and accounted for a higher than average proportion of birth weights at 750-999g (see Table 4.2). The table also reports on the combination of normal/small for gestational age indicators, which are key metrics determining the health status of a VPI population. Calgary has the highest small for GA rate at 22.71%, significantly different from the provincial average of 18.61% ($p<0.01$). The North has one of the lowest percentages of small for gestational age births at 14.08%, significantly different from the provincial average ($p<0.05$).

Most variables outlined in Table 4.3 are relatively constant across health zones, with the exception of an indicator for the diagnosis of any non-malformation. Calgary and South zones had the largest malformation rates (near 40%) while the Central and North zones had the lowest (near 25%). Due to the extreme variability and a skewed mean there are significant differences when comparing the health zones to the provincial average. Over the study period the findings remain stable, except for an upwards trend in multiple births, an indicator for if the mother gave birth to more than one child during delivery. Appendix 7.10 shows the multiple birth rate by zone dramatically rise in 2008/09 from a modest climb from 2004 to 2007.

Table 4.3: Basic Demographics of Very Preterm Infants in Alberta by Health Zone

	Alberta	Calgary	Central	Edmonton	North	South
VPI infants, N	2768	1061	315	918	341	133
Gestational age, wks, mean (SD)	28.8 (2.9)	28.8 (3.0)	29.0 (2.8)	28.8 (2.8)	28.6 (2.8)	28.8 (2.8)
Birth weight, g, mean (SD)	1234 (408)	1212 (413)	1254 (395)	1252 (412)	1251 (403)	1188 (379)
Appropriate for GA (%)	74.53	72.01	74.60	75.93	76.83	78.95
Small for GA (%)	18.61	22.71**	17.14	16.01	14.08*	18.80
Female Gender (%)	47.18	45.90	46.03	48.04	50.44	45.86
Apgar 5 score, mean (SD)	7.2 (2.0)	7.3 (2.1)	7.4 (1.8)	7.1 (2.1)	7.1 (2.0)	7.1 (2.0)
Multiple birth (%)	29.73	28.65	30.79	31.15	27.86	30.83
First Delivery (%)	50.98	51.65	49.84	50.11	52.20	51.13
Malformation, N (%)	887 (32.0)	417 (39.3) **	76 (24.1) **	254 (27.6) *	90 (26.4) *	50 (37.6)
Caesarean delivery (%)	61.2	62.6	56.2	59.8	63.6	66.2

** Statistically significant different (P<0.05) from provincial average*
*** statistically significant different (P<0.01) from provincial average*

4.2 Infant Outcomes

4.2.1 Unadjusted Values

Given the crude study results are directly taken from a provincial dataset, the unadjusted values can be used for population surveillance of the province's neonatal health before adjusting for key risk factors (Table 4.4). The majority of infant mortality occurs during the first 30 days (10.22%) after which the mortality rates climb by ~2% across Alberta to one year after birth. One year mortality rates for VPI is 12.1%, with the highest rate at 14.66% in the North followed by South, Edmonton, Central and then Calgary (9.7%). VPI residing in Calgary stand out given their mortality rate is ~3% lower than any other health zone (p<0.01 for Calgary compared to Edmonton/North). The first hospital length of stay and first hospital episode length of stay differ by approximately 20 days. This shows VPI are being frequently transferred during their stay, either within or outside the hospital; or those who are transferred, have a very large length of stay which creates the 20 day difference between measures. During the first year, VPI on average stay in the hospital for 54 days; this is relatively constant across health zones with the exception being the South having an average of ~58 days (p>0.05).

Table 4.4: Unadjusted Mortality and Length of Stay by Health Zone

	Alberta	Calgary	Central	Edmonton	North	South
	Unadjusted Mortality, N (%)					
30 Day Crude Mortality	283 (10.22)	85 (8.0)*	36 (11.4)	104 (11.3)	43 (12.6)	15 (11.2)
1 Year Crude Mortality	335 (12.10)	103 (9.7)*	40 (12.7)	124 (13.5)	50 (14.6)	18 (13.5)
	Unadjusted Length of Stay, Mean (standard deviation)					
First hospital LoS	28.7 (28.6)	23.0 (27.3) **	26.2 (27.4)	36.2 (29.2) **	29.9 (27.1)	24.0 (30.0)
First hospital episode LoS (continuous, incl. transfers)	51.6 (35.2)	52.0 (34.4)	51.4 (32.8)	51.5 (34.8)	49.1 (38.5)	56.1 (40.1)
First year LoS (not necessarily continuous)	53.6 (38.0)	54.2 (37.2)	53.3 (35.1)	53.2 (37.8)	51.8 (42.1)	57.6 (41.3)
First year NICU LoS (not necessarily continuous)	50.9 (34.5)	50.6 (32.6)	49.5 (31.4)	52.0 (35.7)	49.4 (38.9)	53.9 (35.6)
Avg % of total hospital time in NICU over the first year	94.8%	93.4%	92.9%	97.7% **	95.4%	93.6%

** Statistically significant different (P<0.05) from provincial average*
*** statistically significant different (P<0.01) from provincial average*

When mortality is broken down by GA grouping, Calgary was found to have a very low rate of mortality (48.7%) in infants whose GA is <25 weeks, which is significantly different than other health zones (p<0.01) (Table 4.5). Mortality rates also follow the expected decreasing trend as the gestational age increases. One outlier in this data is the South and North health region's mortality at >32 weeks (20% and 0% respectively); this however may be due to the small sample size of infants (9 in the South and 16 in the North).

Table 4.5: Unadjusted mortality (%) in very preterm infants by gestational age group

Gestational age	Time frame	Alberta (%)	Calgary (%)	Central (%)	Edmonton (%)	North (%)	South (%)
22-24 weeks	**30 days**	62.1	48.7*	78.3	69.6	78.1	70.0
	1 year	65.1	49.6**	82.6	76.0	78.1	80.0
25-26 weeks	**30 days**	13.8	6.6*	17.5	17.6	22.0	5.6
	1 year	17.8	9.0*	20.0	21.6	30.0	11.1
27-28 weeks	**30 days**	6.6	3.5	11.5	7.8	7.4	9.5
	1 year	9.4	7.0	13.5	11.7	7.4	9.5
29-30 weeks	**30 days**	3.1	2.8	2.1	3.7	2.4	5.0
	1 year	4.4	4.3	2.1	5.2	3.5	7.5
31-32 weeks	**30 days**	1.5	1.4	2.5	1.7	0.0	2.9
	1 year	2.1	2.6	2.5	1.7	2.2	2.9
>32 weeks	**30 days**	3.2	2.2	4.0	2.0	0.0	22.2
	1 year	4.8	4.4	8.0	2.0	0.0	22.2

** Statistically significant different (P<0.05) from provincial average*
*** statistically significant different (P<0.01) from provincial average*

4.2.2 Adjusted Length of Stay Results

Table 4.6 provides both adjusted mean hospital episode LOS (HEPLOS) and first year of life LOS among VPI survivors and non-survivors. All length of stay results were adjusted by Level 3 NICU admittance, gestational age, Apgar score, transfer to Level 3 NICU, multiple births, mother's first delivery, any non-lethal malformation, and whether they lived in Calgary/Edmonton (see Appendix 7.11 for model adjustment). When comparing HEPLOS to first year LOS, we found that once discharged from their first hospital episode, the infants are only readmitted for a short duration within a year's time (HEPLOS nearly equals first year of life LOS). For survivors, the longest adjusted mean HEPLOS occurred in the Calgary health region, while the shortest mean length of stay is in the Central health region. There is also a statistically significant difference in length of stay between survivors and non-survivors, with non-survivor's lengths of stay being 24% to 40% of survivor's LOS in each zone ($p<0.01$).

Table 4.7: Adjusted length of stay in very preterm infants by health region

		Health Region of Residence	Length of Stay & 95% CI
Length of stay during the first hospital episode (HEPLOS)	**All**	Alberta	51.69 (50.97-52.41)
	Survivors	Calgary	57.99 (56.4-59.6)
		Central	54.42 (52.0-56.8)
		Edmonton	55.06 (53.5-56.6)
		North	57.96 (55.6-60.3)
		South	57.56 (52.7-62.4)
	Non-Survivors	Calgary	15.40 (11.1-19.7)
		Central	15.84 (8.8-22.9)
		Edmonton	13.54 (10.6-16.5)
		North	16.08 (9.2-22.9)
		South	18.30 (6.9-29.7)
Length of stay (hospital days) during the first year of life	**All**	Alberta	53.73 (52.97-54.49)
	Survivors	Calgary	59.80 (58.1-61.5)
		Central	57.15 (54.5-59.8)
		Edmonton	57.92 (56.3-59.6)
		North	61.47 (58.7-64.3)
		South	59.27 (54.8-63.8)
	Non-Survivors	Calgary	17.62 (12.5-22.8)
		Central	23.21 (12.2-34.2)
		Edmonton	16.73 (12.7-20.8)
		North	24.63 (12.9-36.4)
		South	23.73 (5.6-41.8)

Adjusted by Level 3 NICU admittance, Gestational age, Apgar score, Transfer to Level 3 NICU, Multiple births, Mother's first delivery, any malformation, whether they lived in Calgary/Edmonton

Figure 4.1 and 4.2 graph hospital episode LOS for all VPI (survivors and non-survivors) and the results varied across each health zone. In Calgary the highest adjusted LOS was 52.77 days, while other health zones had lengths of stay between ~50-51 days ($p>0.05$) (Figure 4.1). This longer LOS can be further analysed by GA groups (see Figure 4.2), and it shows the higher LOS in Calgary is seen across all GA groups below 31 weeks, after which the LOS matches other health regions.

Figure 4.1: Adjusted Hospital Episode Length of Stay (days) for Very Preterm Infants by Health Zone (All Patients)

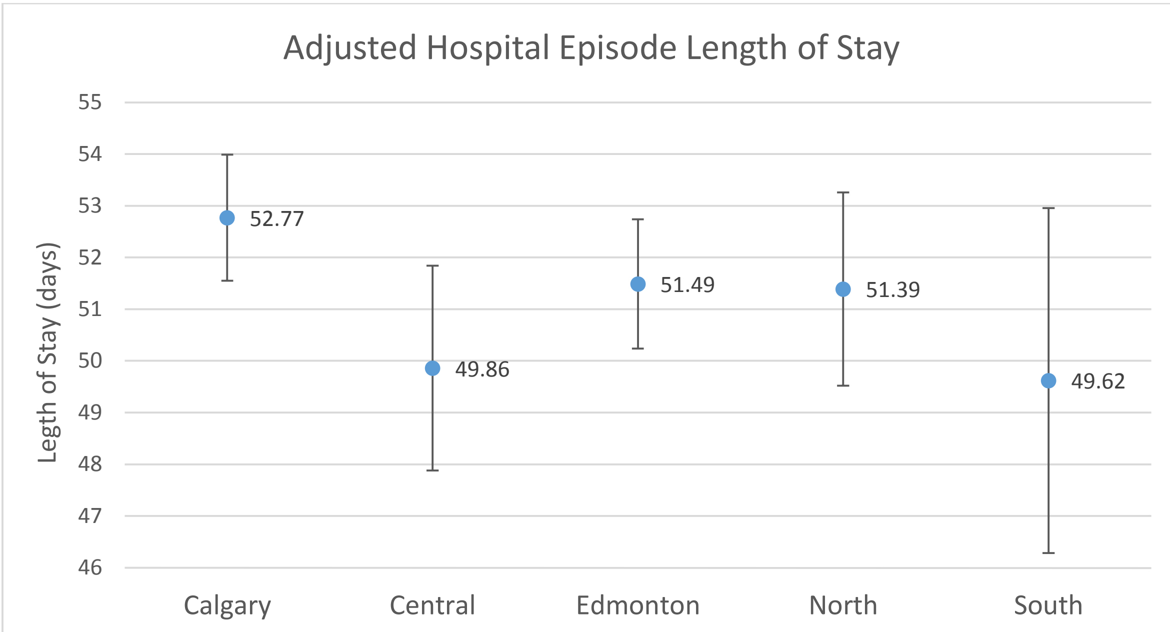
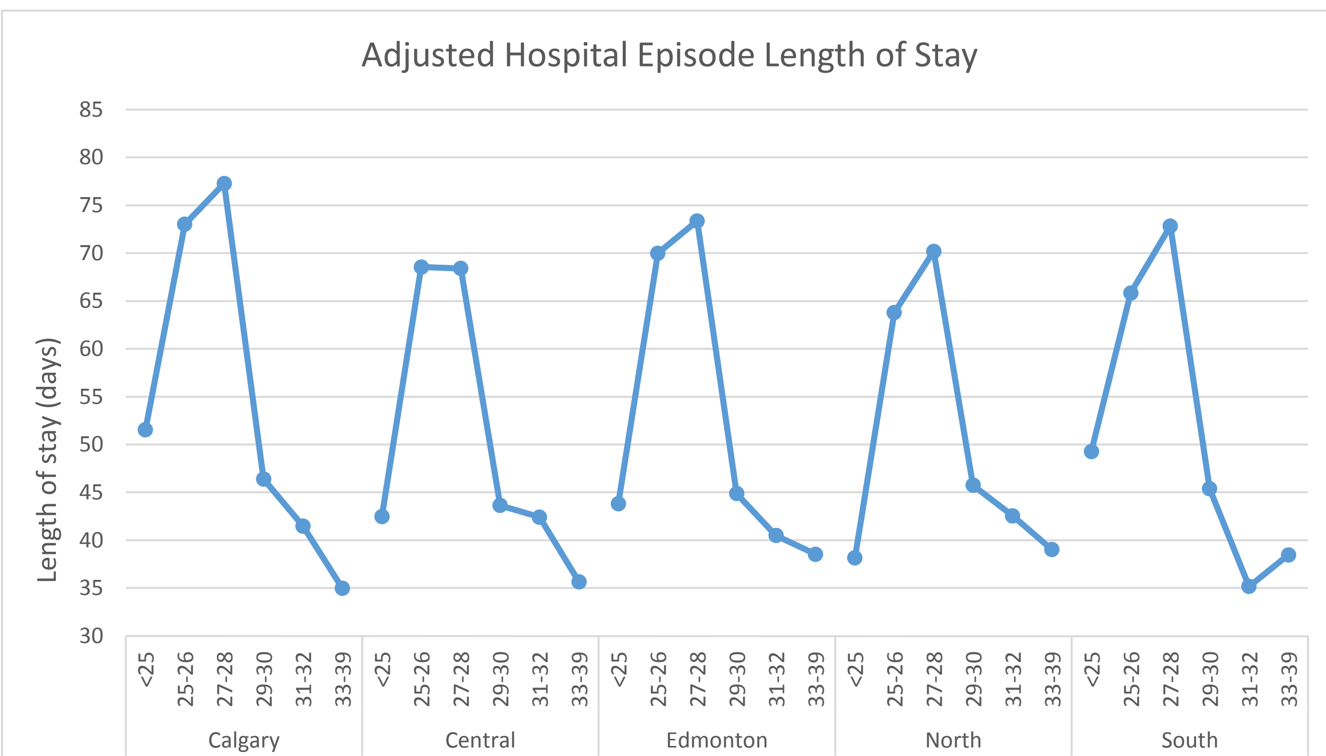
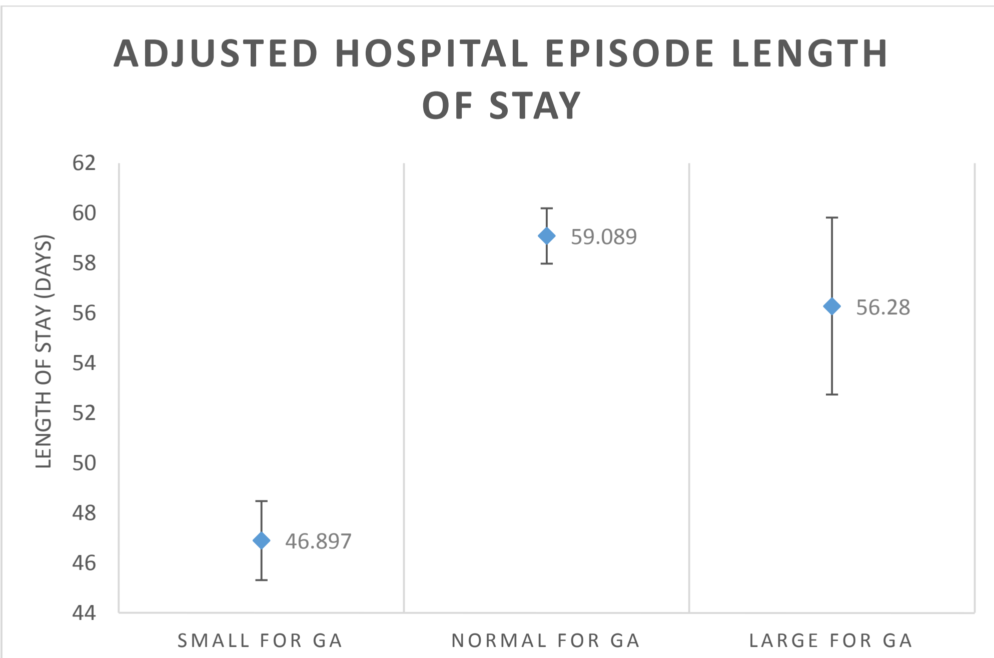


Figure 4.2: Adjusted Hospital Episode Lengths of Stays across Health Zones and Gestational Age Categories



When analyzing birthweight, the study used the Public Health Agency of Canada's preterm infant growth charts to determine if the birth weight for each gestational age was small, normal or large[41]. The results presented in Figure 4.3 show significant differences between the small for GA group when compared to the others ($p<0.001$). Those who are small for their GA have significantly shorter hospital episode lengths of stay than those who were normal or large for their GA (see Figure 4.3's non-overlapping confidence intervals). When these results exclude non-survivors the mean HEPLOS is 47.2, 59.1 and 56.5 for small, normal and large for GA respectively (25.2, 14.6 and 14.0 for non-survivors).

Figure 4.3: Adjusted Hospital Episode Lengths of Stay by Public Health Agency of Canada Birthweight Curves



4.2.3 Adjusted Mortality Results

Adjusted percent mortality at thirty days and one year is graphed in Figures 4.4 and 4.5. All mortality results were adjusted by Level 3 NICU admittance, gestational age, Apgar score, transfer to Level 3 NICU, small for gestational age, multiple births, mother's first delivery, any malformation, and whether they lived in Calgary/Edmonton (see Appendix 7.11 for model adjustment). Adjusted mortality is lowest in Calgary and Edmonton with significant differences in both thirty day and one year mortality occurring between city center zones (Edmonton, Calgary) and the North ($p<0.05$). The North and South had some of the highest one year mortality rates at 15.4% and 13.5%, respectively. The significant differences are unexpected given health regions outside Calgary and Edmonton have smaller sample sizes, which results in wider confidence intervals around the population mean estimate, decreasing the chances for any significant findings.

Figure 4.4: 30 Day Adjusted Percent Mortality by Health Zone for VPI

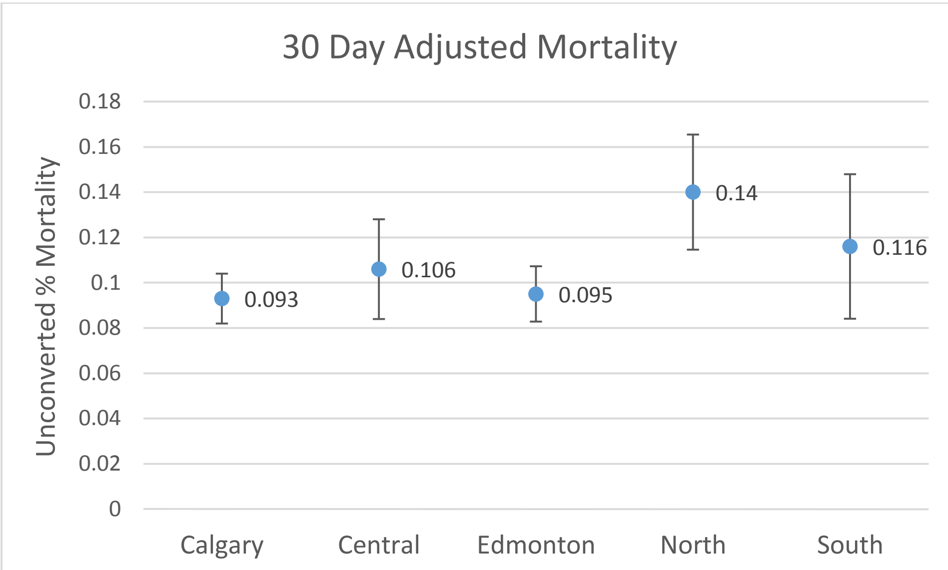
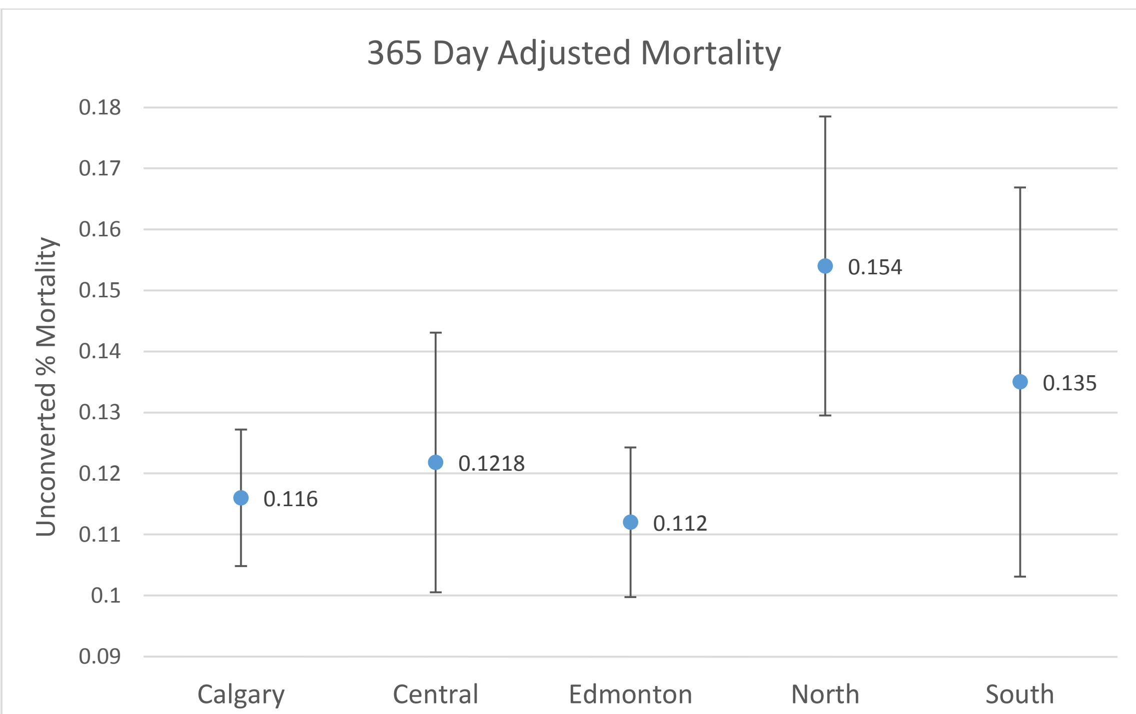
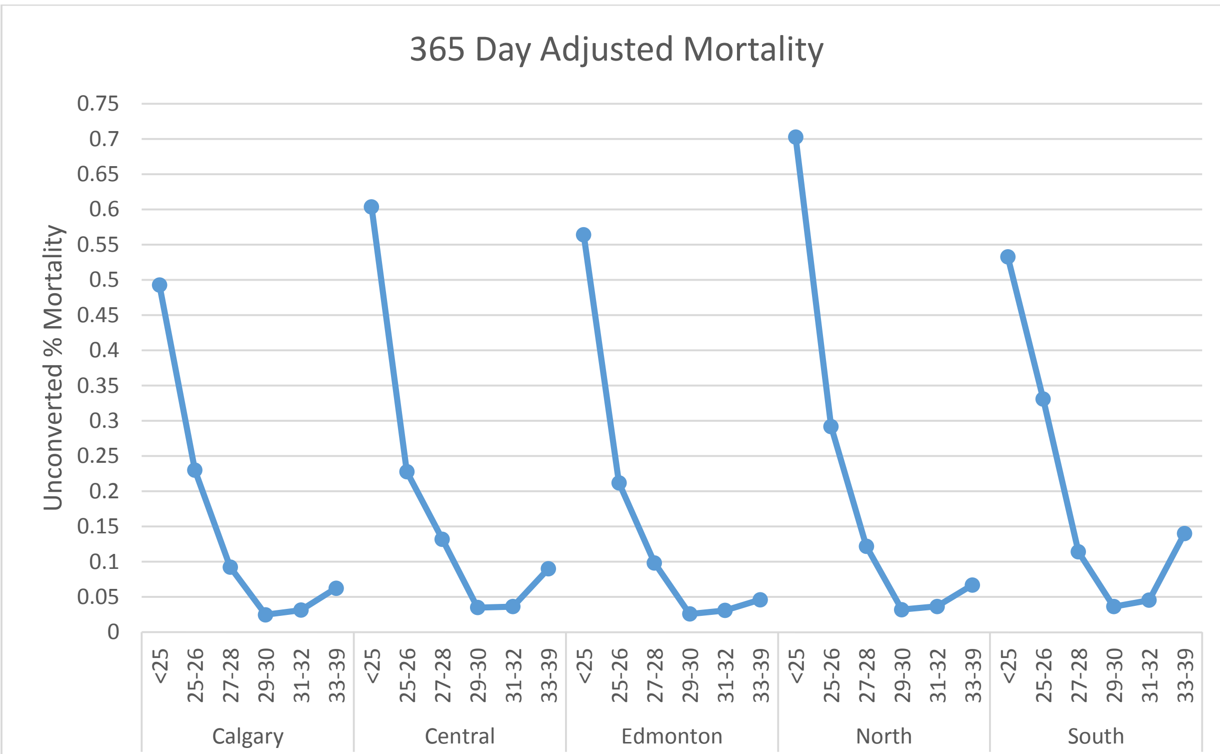


Figure 4.5: 365 Day Adjusted Percent Mortality by Health Zone for VPI



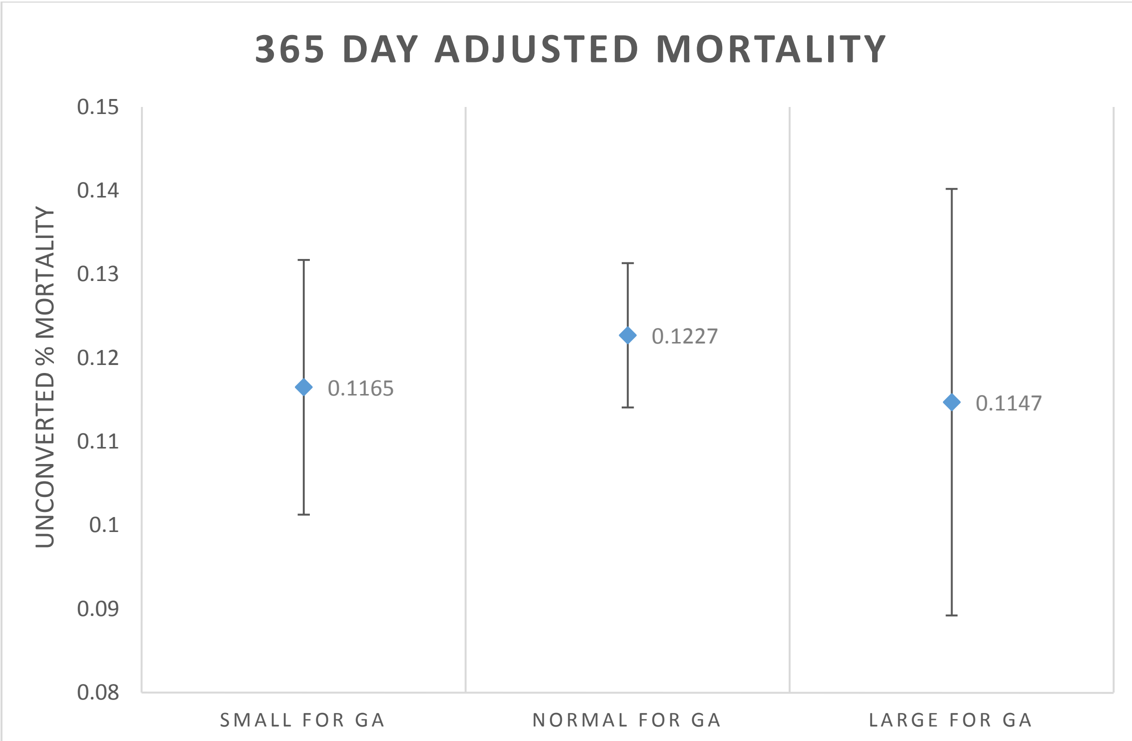
Health zone adjusted mortality rates can be further analyzed when viewing mortality across VPI GA groups. Calgary stands out as a leader in having the lowest mortality rates for the <25 weeks GA group at 49%, 4% units lower than the South and 21% units lower than the North (Figure 4.6). Contrary to an ordinary mortality curve across GA categories, the mortality rates for all health zones in the 33-39 weeks GA group rises instead of decreasing. This rising rate is not unexpected as it represents a high risk subgroup of the population of infants 33-39 weeks GA who are <1500g. In metropolitan health regions with a large sample sizes, the mortality rate from 29-30 weeks GA to 33-39 weeks GA rises ~4% units.

Figure 4.6: 365 Day Adjusted Percent Mortality across Health Zones and Gestational Age Categories



Adjusted mortality by preterm infant growth chart classifications (small/normal/large for GA) fails to find a significant difference across groups, but it does show unexpected mean predicted values (Figure 4.7). The normal for GA group has the highest mortality rate of 12%, while the small for GA has a lower mortality rate of 11.6% (p>0.05).

Figure 4.7: 365 Day Adjusted Mortality by Public Health Agency of Canada Birthweight Curves



4.3 Health Technology Usage/Access

4.3.1 NICU Facility Admission Rates

Clinical guidelines state VPI are to be born in a facility with a Level 3 NICU status in order for these newborns to receive the quality care they require. In the North, 90.6% of all VPI are born in a level three NICU capable hospital, while in Calgary and the South those percentages drop to 78.2% and 75.2% respectively (Table 4.7). Another key metric of determining access to quality care is if the VPI were admitted to any level of a NICU at birth (Level 2 or Level 3). On average 98.5% of VPI in Alberta are born at either NICU level. However there are differences between regions, with Calgary being significantly above the provincial average, while the North and South are significantly below (P<0.01).

Transfer rates were categorized as to or from a level 3 NICU capable hospital (Table 4.7). On average ~6.5% of VPIs are transferred to a level 3 NICU capable hospital, with the highest rates in the Calgary and Central health regions at 7.16 % and 7.30% respectively. The lowest transfer rate was in Edmonton, where only 5.45 % of Edmonton VPI were transferred to a Level 3 NICU capable hospital from any other hospital. Transfers from a level 3 NICU capable hospital to any other lower level hospital was 49.4% for all VPIs in Alberta. The highest rates were observed in Calgary and the South at 64.28% and 63.16% respectively; while the lowest rate was in Edmonton at 30.28%. Another key variable that can act as an indicator for improper hospital level admission is whether the infants is transferred from a level 2 to a level 3 hospital. The Albertan average was 5.31%, but the highest rate was Calgary with 7.07%, significantly higher than the provincial average (p<0.05).

Table 4.7: Very Preterm Infant's NICU Facility Usage by Health Zone

	Alberta	Calgary	Central	Edmonton	North	South
N infants, after exclusions	2768	1061	315	918	341	133
Born at Level 3 NICU Hospital (%)	82.26	78.23**	83.49	84.42	90.62**	75.19*
Born in Level 2 or 3 NICU Hospital (%)	98.48	99.91**	97.78	99.02	94.43**	95.49**
DAD - Initial NICU Admission (%)	93.39	94.16	94.29	93.57	90.32*	91.73
N (%) infants born in non-Level 3 and transferred to Level 3 Hospital next admission	179 (6.47)	76 (7.16)	23 (7.30)	50 (5.45)	21 (6.16)	9(6.77)
N (%) infants ever transferred from Level 3 Hospital to lower level hospital	1,521 (54.95)	751 (70.78)**	196 (62.22)*	308 (33.55)**	175 (51.32)	91 (68.42)**
N (%) infants born in Level 2 and transferred to Level 3 Hospital next admission	147 (5.31)	75 (7.07)*	18 (5.71)	42 (4.58)	5 (1.47)**	7 (5.26)

** Statistically significant different (P<0.05) from provincial average*
*** Statistically significant different (P<0.01) from provincial average*

4.3.2 Proximity to a NICU

With clinical guidelines recommending all VPIs to be born at a level 3 NICU facility, proximity to a facility is a unique factor for understanding mortality and length of stay. Figure 4.8 shows on average the highest mortality (16.1%) is found in those living >300 km from a level 3 NICU facility. However a distinct linear uprising trend is not directly observed, as 201-300 km appears to have one of the lowest mortality rate at 10.6%. A significant difference (p<0.05) in mortality was found between the group living >300km and <20km, which appears to indicate a rising mortality rate as distance increases. The LOS results in Figure 4.9 have no specific pattern or significant differences between distance categories and episode LOS. LOS are between 49-53 days, with hospitals <50km from a level 3 NICU having the longest stay at >52 days. The shortest LOS was found in the 51-100km and 201-300km groups with an average LOS of 49 days.

Figure 4.8: Adjusted 365 Day Mortality by Distance to Nearest NICU Facility

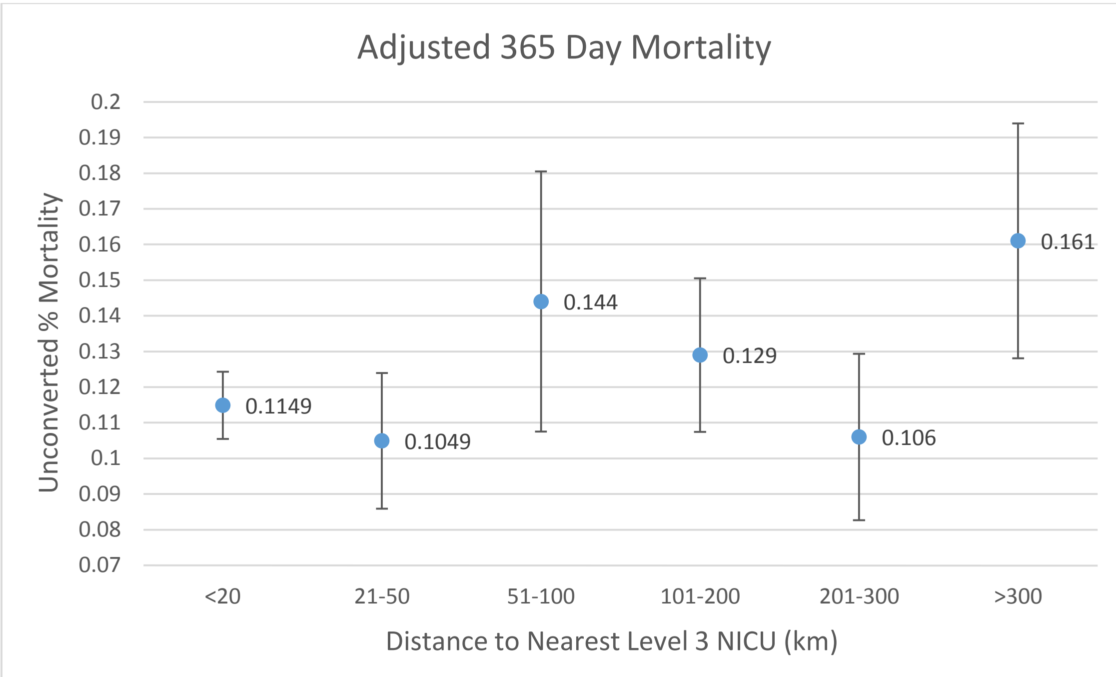
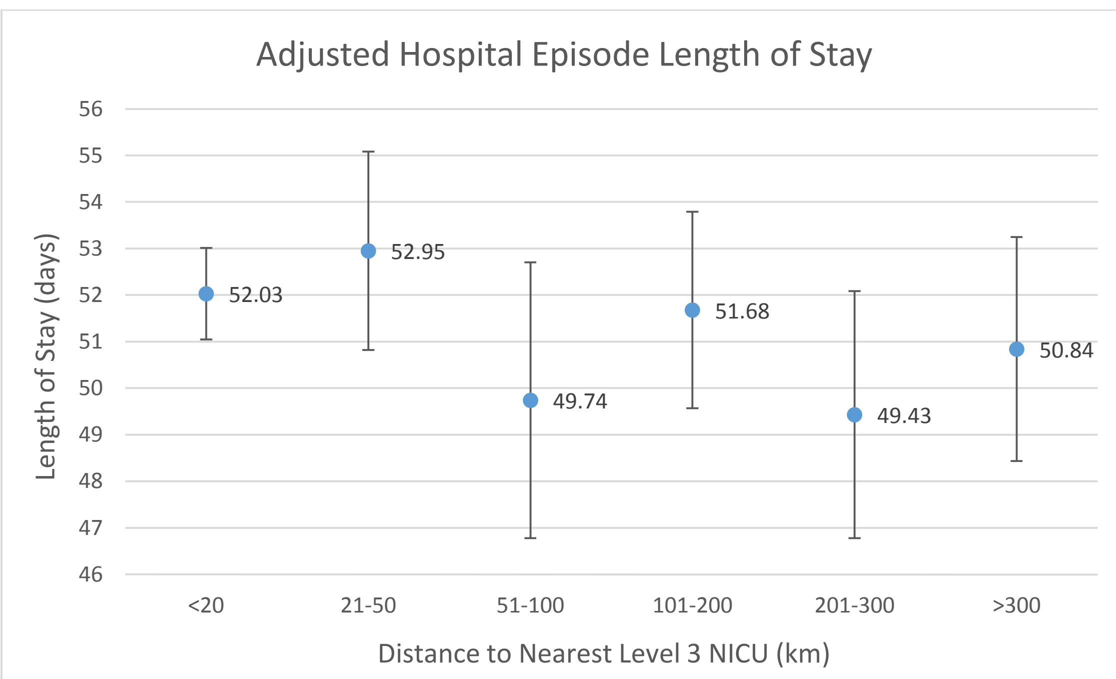


Figure 4.9: Adjusted Hospital Episode Length of Stay by Distance to Nearest NICU Facility



4.3.3 NICU Allocation Model

Currently in Alberta all four level 3 NICU facilities are located within Edmonton and Calgary. This study underwent two different GIS modeling techniques to see if the current system represents an allocatively efficient distribution. Levels 2 and 3 NICU facilities were used as potential future level 3 NICUs, as they would be the easiest to convert or justify as potential future level 3 NICUs.

Modeling to minimize impedance can be seen in Figure 4.10. The model found the current NICU distribution to be allocatively inefficient, and suggested a NICU facility should be established in each health region except the South. The hospitals designated NICU status by the model were: Royal Alexandra Hospital (Edmonton), Red Deer Regional Hospital (Central), Queen Elizabeth II Hospital (North) and the Peter Lougheed Centre (Calgary). Therefore this allocation found in order to minimize driving time to a facility given the locations of VPI over 5 years, Edmonton, Calgary, the North and Central health regions should have a level 3 NICU facility.

The capacitated coverage model can be seen in Figure 4.11, and it found the current NICU distribution to be allocatively efficient. It determined NICU hospitals are best allocated in Calgary and Edmonton in the following hospitals: Royal Alexandra Hospital, Misericordia Community Hospital, Peter Lougheed Centre and Rockyview General Hospital. This model accounts for both NICU facilities' limited bed supply and the minimization of driving time to a facility given the 5 year VPI sample. Therefore the current four level three NICU facilities used today (Royal Alexandra, Stollery Children, Foothills Medical and Alberta Children's Hospital) in Edmonton and Calgary would be near identical to the ones suggested by the model.

Figure 4.10: Model 1 – Allocative Efficiency via Minimized Impedance Model[10]

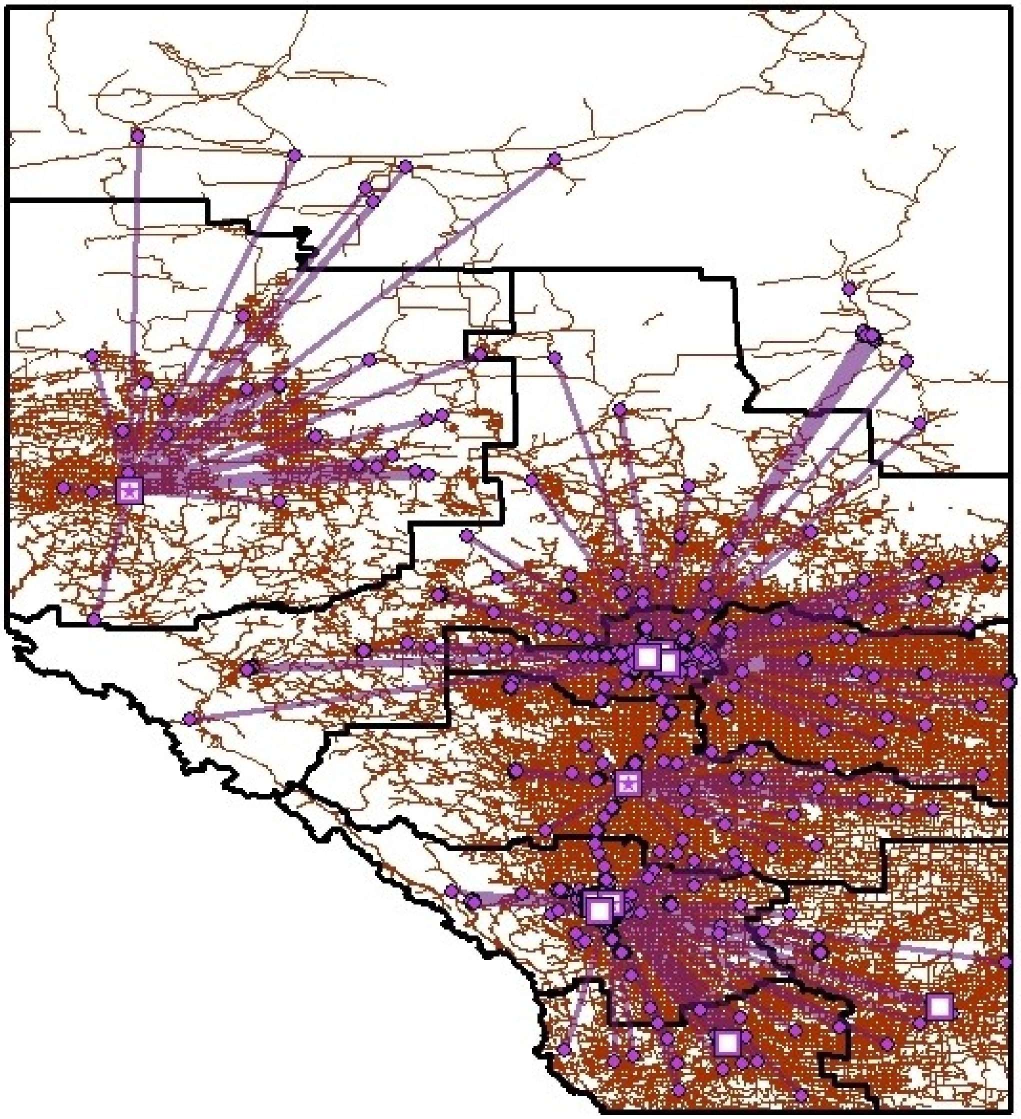
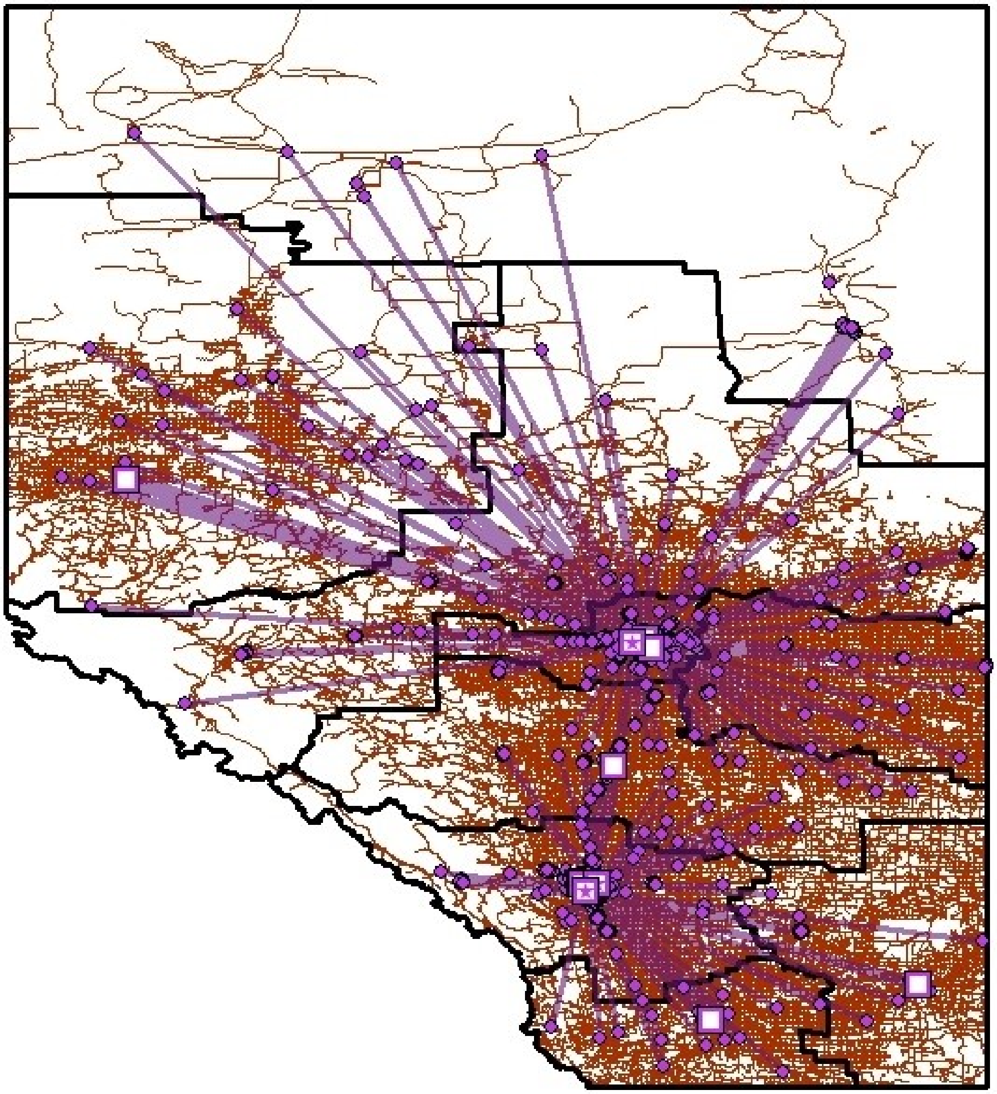


Figure 4.11: Model 2 - Allocative Efficiency via Capacitated Coverage[10]



4.4 Resource Impact

4.4.1 Costing Data Summary

The distribution of total costs for VPI over the study period is displayed in Figure 4.12 with a box plot. The first, second and third quartile are $42,700, $64,600 and $140,400. The data is right skewed, where a long tail of high scores pull the mean ($94,000) above the median ($64,600). This skew can be seen in Figure 4.13, as there is a large number of outliers above the upper adjacent value (~$240,000). Given the percentile distribution and the 95'th percentile being greater than $240,000, over 5% of the data is considered an outlier, which skews the total cost distribution.

Figure 4.12: Box Plot of Total VPI Hospital Costs Excluding Outliers

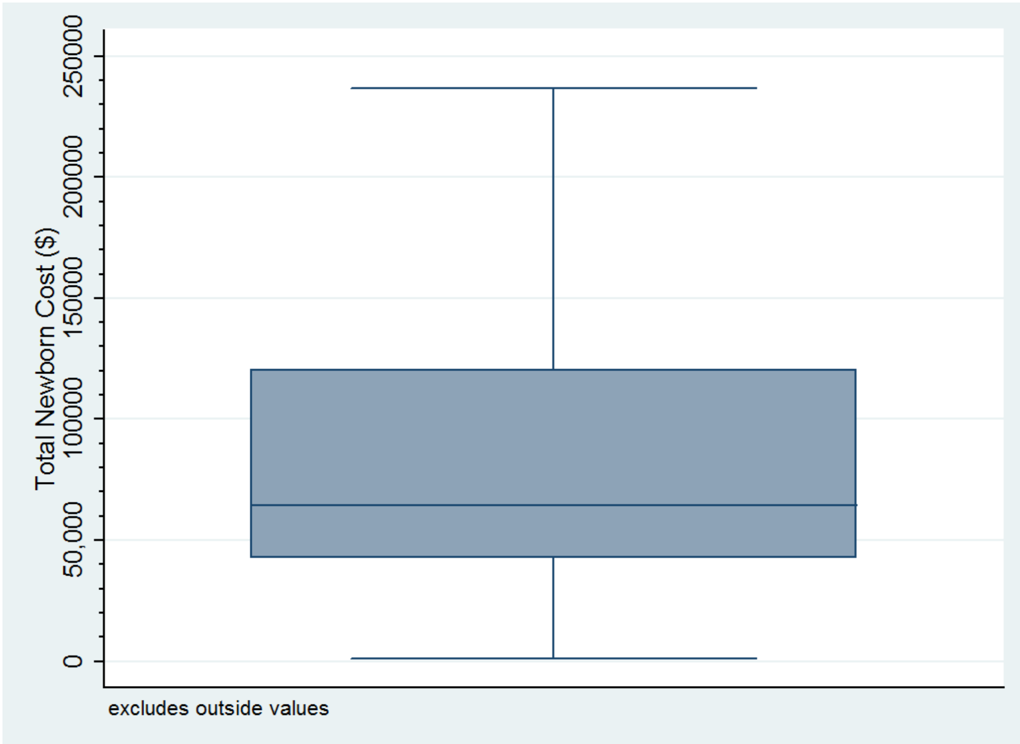
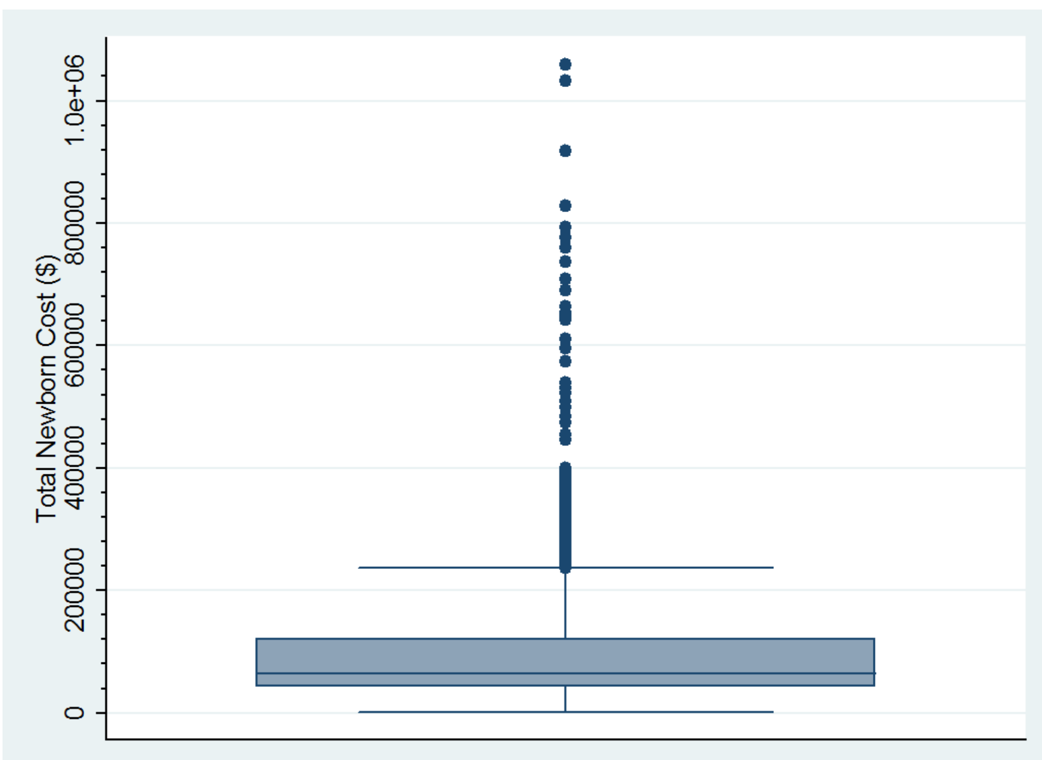


Figure 4.13: Box Plot of total VPI Hospital Costs Including Outliers



4.4.1 Cost Relationships

Several key cost relationships were explored in this study, with the aim to see how distance to a level 3 NICU and gestational age at birth impact overall cost. The relationship between distance to nearest NICU and cost can be observed in Figure 4.14, and no clear trend can be observed. When viewing gestational age's relationship to cost in Figure 4.15, it is apparent at a low gestational age (<25 weeks) there are the highest one year costs, and these costs decrease with every increase in gestational age. These results were confirmed in the Generalized Linear Model (GLM), as gestational age was a significant predictor ($p<0.001$) while distance to the nearest NICU was not.

Figure 4.14: Crude Total Year Hospitalization Costs by Distance to Nearest Level 3 NICU in Very Preterm Infants

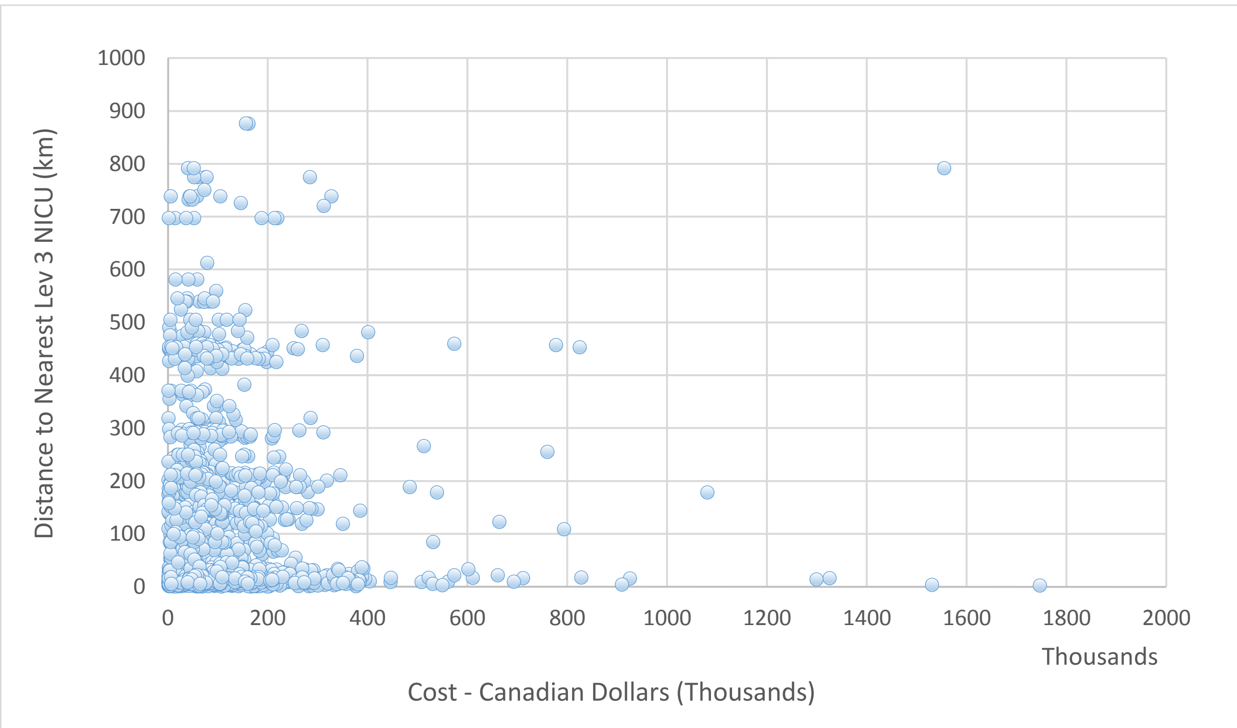
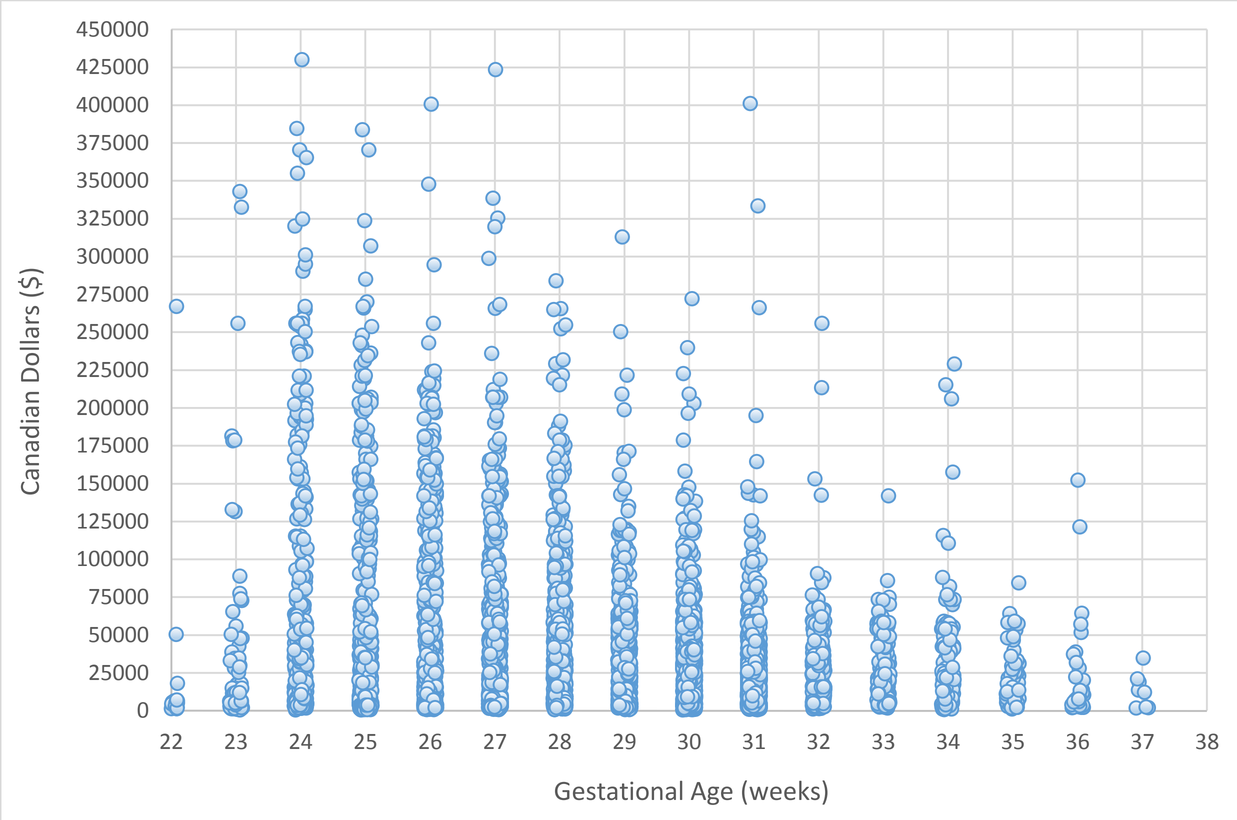


Figure 4.15: Crude Total Year Hospitalization Costs by Gestational Age in Very Preterm Infants



The GLM model seen in Table 4.8 shows the costing model used to explore distances' relationship to total inpatient costs. Each model number represents an additional variable being added into the GLM model on hospitalization costs (stepwise regression approach). Models 7 and 8 are identical to Model 6 except for the restrictions of including only survivors or non-survivors. Continuous and categorical variables for distance were used but are not shown in Figure 4.8's stepwise regression as they were all insignificant (p>0.05). Although living in the city (Edmonton or Calgary) was a significant predictor in mortality and LOS models, it had an insignificant p-value of 0.261 in the cost model. When the model only included those VPI who died within the first year, it found having a gestational age of 22-25 weeks, being small for their gestational age and having a malformation were no longer significant predictors for cost. When the model only included VPI survivors, both having a gestational age of 22-25 weeks and having an Apgar 5 score of 1-5 were no longer significant predictors for cost. Modified Park Test was used to test the GLM model goodness of fit statistics. The test statistics reaffirm the appropriate use of a gamma distribution in the GLM, as a coefficient of 2 indicates a gamma distribution best fits the data, and the variance is proportional to square of mean.

Table 4.8: Parameter Estimates of Log Transformed Hospitalization Costs using Stepwise GLM Modelling

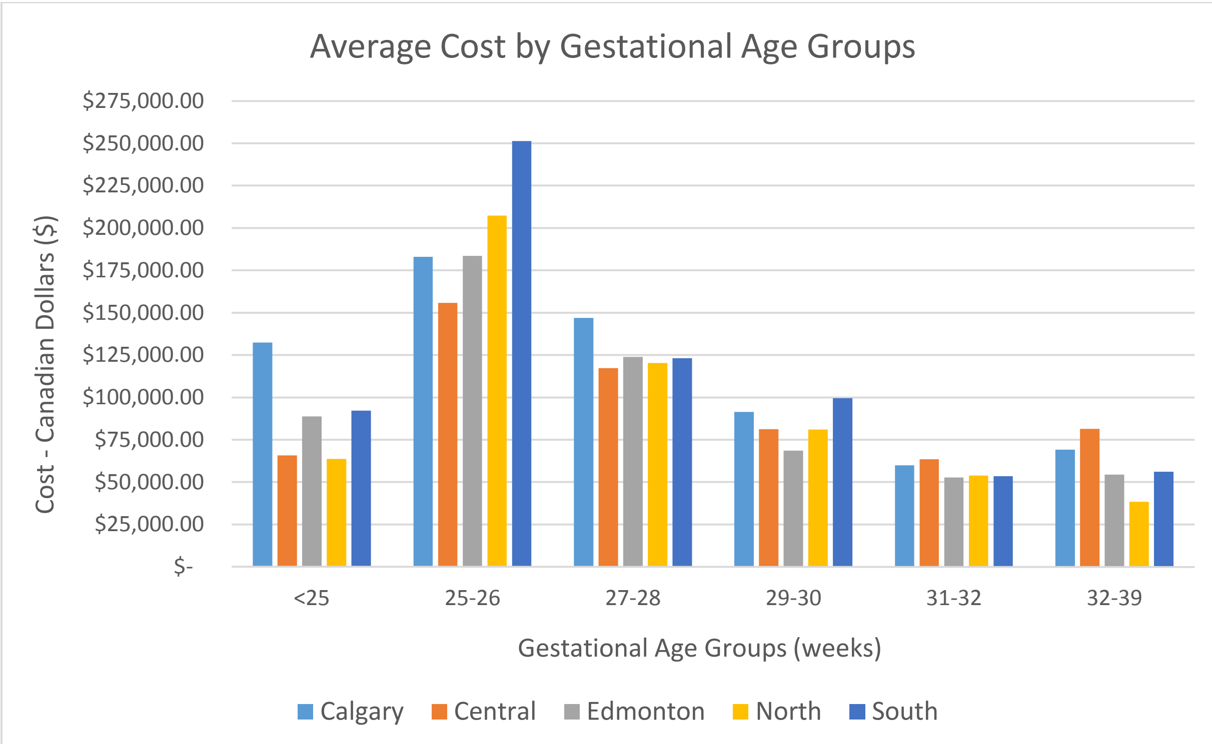
Variable	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Only Deaths	No Deaths
GA 22-25	0.42	-0.40	-0.39	-0.30	-0.32	-0.33	-0.19*	0.008*
Hosp. Ep LOS		0.023	0.023	0.023	0.022	0.022	0.031	0.017
Admitted to Level 3 NICU			0.043*	0.061*	0.24	0.24	0.98	0.20
Sga + Apgar 5 score 1-5				0.15 + -0.26	0.18 + -0.27	0.18 + -0.27	-0.10* + -0.36*	0.19 + 0.009*
Transfer to Level 3 + Any Malformation					0.45 + 0.098	0.45 + 0.096	1.42 + 0.17*	0.40 + 0.11
Living in City (Edm or Calg)						0.029*	0.11*	-.002*

** P value is greater than 0.05*
Note: all other P values are less than 0.001
Modified Park Test=2.000339

4.4.2 Cost Estimates

When stratifying by gestational age and health zone, the data shows where the highest costs are accumulated and by whom. The 25-26 weeks GA group has the highest costs at well over $150,000 per VPI in all health zones. Of that group the highest average hospital cost is in the South, with an average annual cost for a VPI at $250,000, followed by the North at $207,000 (p>0.05). Due to the high mortality rate in infants <25 weeks GA the costs are relatively low when compared to older GA groups. Within the <25 weeks GA group Calgary has a significantly higher cost per VPI than any other region at ~$125K, which is $40,000 more than the next highest region (Figure 4.16).

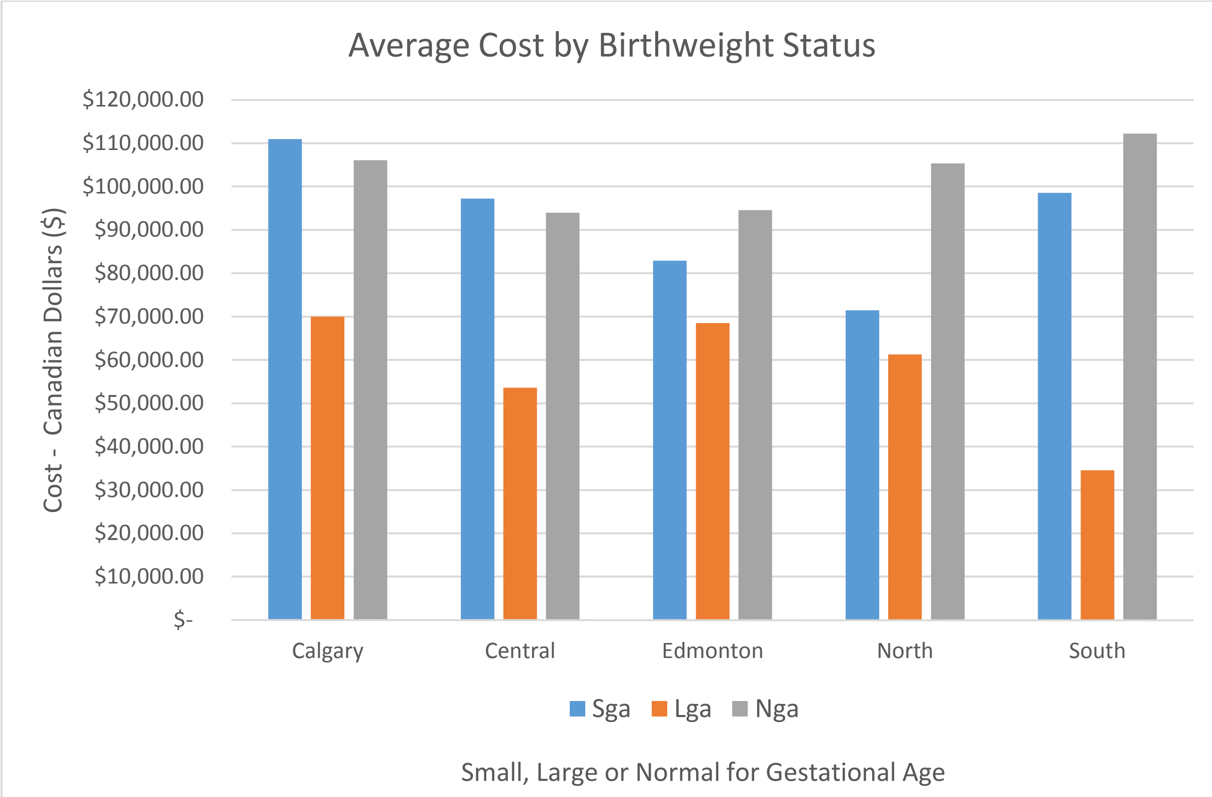
Figure 4.16: Average Hospital Costs in Very Preterm Infants by Gestational Age Groups and Health Zones



**Costs standardized to 2010 Canadian dollars*

The average cost per VPI by birthweight classification reveals large differences. The large for gestational age group has significantly lower costs in the South, Central and Calgary health zones (Figure 4.17). The highest average cost per health zone fluctuates between normal for GA and small for GA. Between health zones the rates are quite different, but within the North and South zones the small for GA costs are much lower than the normal for GA costs.

Figure 4.17: Average Hospital Costs in Very Preterm Infants by Birth Weight Groups and Health Zones



**Costs standardized to 2010 Canadian dollars*

4.4.3 Budget Impact Analysis

Over the study duration it was found that on average the annual cost for all very preterm infants in Alberta is $52,040,000 (2010 as dollar reference). This is further explained in Table 4.9, which shows the cost for all VPI over 5 years was ~260 million dollars. The major drivers of these costs were Calgary and Edmonton, due to population dynamics and the large number of VPIs residing in these health zones. Despite these regions having the highest overall costs, it did not necessarily mean they had the highest average cost per VPI (see Figure 4.16). The South and Calgary had an average cost per VPI far greater than the provincial average (~$10,000). The single highest hospitalization costs from an infant were in Calgary and the North, at just over one million dollars. Table 4.10 shows average costs by health zone and fiscal year, and a rising trend was observed from 2004/05 to 2008/09 with the exception of Calgary. Costs do not incrementally rise each year but instead fluctuate, this can be seen in costs jumping drastically in 2008/09 after a low costing year in 2007/08.

Table 4.9: Average and Total Hospital Costs by Health Zone in Very Preterm Infants

Health Zone	# VPI	Total Cost of VPI over 5 Years	Average Cost per VPI
Alberta	2768	$ 260,200,000	$ 94,003
Calgary	1061	$ 108,000,000	$ 101,791
Central	315	$ 28,000,000	$ 88,889
Edmonton	918	$ 78,500,000	$ 85,512
North	341	$ 31,500,000	$ 92,375
South	133	$ 14,200,000	$ 106,767

**Costs standardized to 2010 Canadian dollars*

Table 4.10: Average Hospital Costs per VPI by Health Zone and Fiscal Year

Health Zone	2004/05	2005/06	2006/07	2007/08	2008/09
Alberta	97,094	88,947	97,899	85,040	100,946
Calgary	102,222	101,795	111,889	92,849	101,282
Central	89,444	88,330	90,722	82,710	93,817
Edmonton	94,996	72,678	86,588	75,308	96,154
North	92,343	80,236	83,060	79,399	111,565
South	101,705	105,776	110,497	110,901	108,508

**Costs standardized to 2010 Canadian dollars*

5 Discussion

5.1 Summary Statistics

The summary statistics have critical information on the study population, and how certain risk factors have a greater impact on health, technology and costing outcomes. As the yearly rates were quite stable over the study period, the average annual results were reported. As previously highlighted Calgary has the most infants in the lowest birth weight (3.2%) and GA categories (11%). This coupled with the fact their small for gestational rate is the highest of the population at 22.7% has drastic effects on population health outcomes. This is due to the fact preterm infants less than 25 weeks GA and extremely low birth weight have an increased rate of mortality[25]. This also could provide two extremes in length of stay measures, where the infant passes away shortly after birth, or extensive treatment and therapy requires them to stay in hospital for a long period of time. The study also found given the inclusion criteria for the VPI population as VLBW or VLGA, there was an increased proportion of infants small for gestational age at >32 weeks. This dynamic skews the unadjusted >32 weeks GA group from the population average, as these infants are more mature and would have a higher survival and lower overall LOS. Another key result that required adjustment was whether the infant was born or treated in a level 3 NICU. In the literature review it was shown those born in a level 3 NICU have the best health outcomes, this was reaffirmed in the study as unadjusted mortality in a level 3 facility was 11% and 16.5% in a level 2 facility. There was also variability within level 2 facilities located within or outside the city (Calgary/Edmonton), with a 31% mortality rate outside the city and 17% within. These variations demonstrate why the adjustment done in the study is so important when attempting to compare health outcomes across differing health zones, facilities and gestational ages.

The malformation rates followed a standardized definition, however this broad definition disregards the severity of malformations. Lethal congenital malformations were excluded early on but all other malformations were calculated using ICD-10 coding of any diagnostic code that were “Q00-Q89”. This grouping of malformations was conducted to match a European study’s methodology, and allow for later comparisons across adjusted values given similar model adjustment[37]. As found in Table 4.3 the malformation rate in Albertan VPI was 32%, the European comparator study found malformation rates of 3.1%, 15.5%, and 12.9% in Finland, Italy, and Norway respectively[37].

5.2 Infant Outcomes

The adjusted mortality results found a common increase in mortality in VPI from 31-32 weeks to 33-39 across all health zones. This rate doubled in the North and Central, while the South due to sample size limitations showed an unreasonably steep climb. The increased mortality rate in the 33-39 weeks GA groups can be explained by how VPI were defined, as although this subgroup includes gestationally mature infants, they are all <1500g and 99.47% are SGA. This explanation may to a lesser extent also explain the 31-32 weeks GA category, as the SGA rate rise to 19.9%, an absolute increase of 10% when compared to all lower gestational age groups.

The adjusted LOS provided noteworthy findings showing that there may have been a different approach to treat VPI in each health zone. Calgary had the longest average LOS for surviving infants while Edmonton had one of the shortest. Since these results are adjusted for severity through factors like gestational age and whether they were small for their GA, it may indicate different treatment approaches between Calgary and Edmonton NICUs. Statistical significance was not found when stratifying across gestational age groups due to sample size limitations; but simple observations such as a nine day longer HEPLOS in VPI <25 weeks GA in Calgary compared to Edmonton reinforce the possibility of differing treatment approaches. This information coupled with the fact Calgary had a 7% lower mortality rate in infants <25 weeks GA may warrant an in-depth evaluation into the different health zone's treatment strategies.

Contrary to most of the literature, adjusted HEPLOS was significantly shorter in the small for gestational age (SGA) group when compared to the normal for gestational age (NGA) group. This same distinction was not apparent in the 365 day mortality comparison, although the mean mortality for NGA was insignificantly higher (12% vs. 11.4%). In one Canadian study on preterm (<33 weeks GA) infants, the SGA group had a mean LOS of 50 days, while the non-SGA group was 40 days[59]. This would be the exact opposite of our findings, however one fundamental difference exists between these studies, the study's inclusion criteria included both VLBW and VLGA. Therefore for a true direct comparison this study would have to only be looking at infants <33 weeks, as the current distribution has a large proportion of SGA infants at higher gestational ages (would result in a lowered mortality and LOS).

Through international collaborations, the study's methodology closely resembled the EuroHOPE working group[37]. This allowed for an international comparisons with near identical statistical adjustments and inclusion/exclusion criteria (see Table 5.1). Albertan VPI mortality (12.1%) was similar to Finland and the Netherlands at 12.9% and 13.1% respectively; but far from the Sweden, Scotland and Norway at 8.0%, 6.3% and 5.5% respectively (although this mortality rate appears satisfactory, greater research into low VPI mortality countries' clinical guidelines and best practices should be explored in order to bridge the gap). However the EuroHOPE data was not without its limitations, and several countries based on policies or data linkage issues were thought to have underestimated mortality rates. The Netherlands had a low linkage rate that disproportionately excluded high risk multiple birth infants. While Scotland's mortality rates were believed to be underestimated due to poor linkages, where unlinked data had lower Apgar scores and GA that correlate with higher mortality risk[37]. The Albertan hospital episode length of stay (HEPLOS) had similar results to the mortality rates when compared internationally, although lower lengths of stay in countries like the Netherlands may not be attainable in Alberta due to widely different policies on the treatment/services provided for infants born at extremely low gestational ages. The Netherlands national guidelines recommend active treatment only for infants >24 weeks GA, and palliative care for infants <25 weeks; which would worsen mortality rates for infants <25 weeks GA and decrease their recorded LOS[37]. As seen in Table 5.1 Alberta lags behind in the percent of VPI being born at a level 3 NICU facility, although both Alberta and most of the international community failed to meet the Healthy Peoples 2010 goal of having 90% of VPI being born at a level 3 facility[33].

Table 5.1: Albertan health outcomes of VPI compared to multiple countries[37]

Crude rates	**Alberta**	**Finland**	**Hungary**	**Italy**	**Netherlands**	**Scotland**	***Sweden (linkable)**	***Norway (linkable)**
1 year mort. rate	12.1%	12.9%	18.1%	13.8%	13.1%	6.3%	8.0 %	5.5%
Average hospital episode LoS	51.7	47.1	46.0	59.1	31.7	35.2	65.7	32.2
Born at a level NICU 3 facility	82.3%	79.0%	89.9%	93.0%	NA	NA	52.7%	96.7%

Source: Numerato, 2015
**Follow-up treatment for one year was only available for ~60% of infants, which caused a bias that downwardly skewed mortality rates*

5.3 Health Technology Usage

The neonatal health system in Alberta is lagging behind some international performance standards. 82.3% of Albertan VPI are born in a level three NICU hospital, this rate is far from leading the international community. France and Georgia have rates of 71% and 77% respectively, while Finland and California had rates of 88%, and 90% respectively[18, 37]. However the Albertan percentage is greater than published literature on the Canadian average, as a Canadian study looking at VLBW infants across Canada from 2006-2008 found only 75% of VLBW infants were admitted to a level three NICU[25]. The low level of VPI born at a level 3 NICU in Calgary (78%) is difficult to explain given the accessibility to Foothills Medical Centre; however the lower rates may be due to overcrowding, as they have a 2% higher rate on average of infants from a level 2 facility being transferred to a level 3 facility. The overcrowding theory is also reinforced by the shorter initial hospital stay and high transfer rate from a level 3 to level 2 facility. The transfer rates are much higher in Calgary (64%) and the South (63%) compared to Edmonton (30%) and the North (45%). However the low level three admittance rate in Calgary may be much higher today given the opening of Alberta Children's Hospital in Calgary and the availability of more level 3 NICU beds. Despite the subpar scores in level 3 admittance rates for VPI, the NICU admittance rates to either a level 2 or 3 facility were 98.5% for the province. Therefore VPI in Alberta are being screened and sent to acute care facilities, but improvements need to be made in ensuring mothers deliver VPI at the required level 3 NICU.

Transfer rates across the province vary by health region and provide key evidence to evaluate overall system performance. Transfers to a level 3 facility average 6.5% in the province with the highest values being 7% in Calgary followed by Central and South, while the lowest being Edmonton and the North. The same three health regions hold the highest transfers rates from a level 2 to a level 3 facility; and this could indicate a lack of available NICU beds in Calgary to support the demand during the study time period. This is also reflected in the high number of infants being transferred from a level 3 to a lower level facility in the same regions (Calgary, Central and South at 70.8%, 62.2% and 68.4% respectively). By having a higher percent of infant being transferred out of a level 3 facility, it may indicate a shorter turn around or a push out of a high level facility due to incoming demands. To note the transfers from a level 3 to lower level facility may be higher for Edmonton and the North due to the Royal Alexandra Hospital being both a level 3 and level 2 facility. Unfortunately the study is unable to distinguish between a level 3 or a level 2 NICU admission in the same hospital, and cannot measure these unique types of transfers. A factor that would increase transfers to a level two facility in the South is their two level 2 NICU facilities; so families and physicians may advocate for a transfer from a level 3 facility to a level 2 facility in the South so they are closer to their home.

The relationship between NICU proximity and length of stay was non-existent, however, a complex relationship was observed between NICU proximity and VPI mortality. One year mortality was highest at 16.1% in infants living >300km from a level 3 NICU facility, and a weak positive relationship was observed in Figure 4.8 when plotting adjusted mortality with rising distance to nearest level 3 NICU categories. In addition to this relationship the model found those living in a metro area (Calgary, Edmonton) had significantly lower odds of mortality (OR = 0.71) when compared to non-metro areas (North, South, Central) ($p<0.05$). This finding and the 99% average an infant is born in a high level NICU (Level 2 or 3) in Calgary and Edmonton coincides with literature finding VLGA infants who are not delivered at a level 3 facility have a higher odds of living outside a metropolitan area[18]. This finding also further validates the use of distance modeling to optimize NICU allocation, given living in a city centre (where level 3 facilities are primarily located) is a significant predictor of VPI mortality.

Models of allocative efficiency gave differing interpretations depending on the criteria used for defining what is allocatively efficient. The net result is the current NICU allocation is acceptable, given the geographical demand and the limited bed capacity of each facility. The model of minimized impedance may warrant future review as the population of Alberta evolves. Future research should continue to evaluate causal or clinically significant relationship between distance to the nearest NICU and another key indicator (mortality, NICU admittance rates, costs, LOS, morbidity) in order to continue to support the model of care that best represent the health system and population's needs. In our study we found living in a metropolitan centre is associated with a higher odds of survival, so further research into this relationship should be pursued in order to better serve the non-metros of Alberta. To note, the GIS models used are not without their limitations, and ideally the model would determine allocative efficiency on more than just distance. More advanced modeling should also include data on mortality, LOS, costs, workforce limitations, and NICU admittance rates. These variables explain the complex relationship of allocative efficiency, such as a NICU treating less than 100 patients per year have been shown to have an odds ratio of death of 1.78 when compared to NICUs treating more than 100 patients per year[8].

5.4 Resource Impact

Several costing relationships were observed to justify the use of the allocative efficiency distance models. The study failed to find any significant relationship between costs and distance to the nearest NICU. This can be observed in Figure 4.14 and the GLM results of a continuous distance variable having a p-value of 0.595. Variations of evaluating distance's relationship to inpatient cost were unsuccessful, such as those living in Edmonton or Calgary were not shown to have higher/lower costs than those living outside the city. These results indicate distance to a level 3 NICU facility is not a key driver for hospital inpatient costs, and those living far from a level 3 NICU facility do not have significantly higher inpatient costs. However, there may be other costs this study could not measure, such as hospital transfer costs of those mothers who were not initially admitted to a level 3 facility.

Roughly 54 million dollars was spent per year on VPI infants, and this amount is expected to rise given an increasing trend of VPI births from 2005-2008 (see Appendix 7.5 & 7.6). From 2005 to 2008 the VPI birth rate jumped from 450 to 650 infants per year; this may have significant policy implications and at the very least should be monitored. Given Alberta Health Services 2010 budget, VPI account for 2.12% of the Inpatient acute nursing care services budget[1]. This percentage could rise as the 82% level 3 NICU admission rate rose closer to 100%, as the average level 3 NICU admission in our study had a resource intensity weight double the size of a level 2 NICU admission. Although the AHS budget proportion appears low, the average cost per VPI is $94,000, with considerable variation between health regions. The average cost per VPI is $15,000 higher in Calgary compared to Edmonton, and is almost $10,000 above the provincial average. In order to contain costs, provincial guidelines on treatment strategies or management strategies at the time of discharge should be implemented, as there appears to be considerable variation in length of stay and mortality rates despite adjustment for case severity.

5.5 Strengths & Weaknesses

Although the study actively and methodologically attempted to minimize study limitations, several factors may have had an impact on the overall validity of the study. The costing ideally should have taken a societal perspective, to include all direct and indirect costs, instead of only using the available hospital costs. This gold standard became near impossible to replicate due to the funding arrangement between neonatal specialists and Alberta Health. Specialists are not reimbursed on a fee-for-service basis but are instead paid through an alternate relationship plan (ARP). This reimbursement method creates issues in the Physician Claims database, where procedures and technology usage is not documented reliability/appropriately. Another limitation in not taking a societal perspective is the inability to measure lost productivity costs of family members taking time off work to visit the hospital, and the additional costs accrued through lodgings, parking and transportation expenses. Another limitation with the data is the study period does not perfectly reflect practice today. In the study, the Alberta Children's Hospital was not yet operating, and the addition of these NICU services and beds may have changed health outcomes across the province and health zones (reduced external generalizability). Another issue with the study period is that it may not represent the rapidly changing population dynamics of Alberta. Within the last five years the North and Edmonton health zones have seen rapid growth, which may warrant the discussion for additional neonatal health resources. An additional limitation is the inability to analyse links between acute services and community services that might facilitate shorter length of stays for VPI. The assessment is also limited to short term outcomes (one year) and cannot measure long-term neonatal morbidities or neurodevelopmental outcomes that are associated with VPI. Measurements of these long-term outcomes would provide an accurate representation of the complete economic burden VPI can have. However, literature on the long-term costs find the initial hospital stay comprise 79.5% of the total 4-year hospitals costs in VPI[30].

Despite the provided limitations, the study was based on well-established methodological practises used in the literature, and contained a study population which encompassed the vast majority of all Albertan births (improves external validity). The use of provincial databases within the study also provided a large sample size, which made it possible to stratify by gestational age groups to better analyze morbidity and mortality without losing significant study power.

5.6 Conclusion

The study found significant variation in health outcomes, service utilization and costs across Alberta's health regions. A unified treatment strategy for very preterm infants could help reduce the variability and improve service utilization and cost containment. There are several key policy implications, as the current NICU facility allocation should be further evaluated in future studies to ensure the current system is optimized to improve patient outcomes. This study also introduces a unique method for allocating health facilities that could be adopted in the facility planning process; as current research indicates oftentimes these decisions lack an objective methodology and are instead based on political influence and/or guesswork[19].

6 References

1. Alberta Health Services (2010). Operating Budget and Business Plan 2010/2011. Retrieved from: http://www.albertahealthservices.ca/Publications/ahs-pub-2010-06-29-budget-businessplan.pdf
2. Alberta Health Services (2015). Capital Projects: Retrieved from: http://www.albertahealthservices.ca/capitalprojects.asp
3. Alberta Health (2015). Overview of Administrative Health Databases. http://www.health.alberta.ca/documents/Research-Health-Datasets.pdf.
4. Alberta Perinatal Health Program (2006). Information Management and Research. http://www.aphp.ca/infomgmt.html.
5. Alberta Reproductive Health Report (ARHR) (2011). Alberta Reproductive Health: Pregnancies and Births Table Update 2011. Edmonton, AB: Alberta Health and Wellness.
6. Aly, H., Hoffman, H., El-Dib, M., Said, L., Mohamed, M. (2014). Factors affecting length of stay in late preterm infants: an US national database study J Matern Fetal Neonatal Med, 1476-4954
7. American Academy of Pediatrics (2008). Hospital Discharge of the High-Risk Neonate. Pediatrics, 122(5).
8. American Academy of Pediatrics (2012). Levels of Neonatal Care. Pediatrics, 130(3).
9. Ananth, C.V., Liu, S., Joseph, K.S., Kramer, M.S. (2009). A comparison of foetal and infant mortality in the United States and Canada. International Journal of Epidemiology. 38, 480-489
10. Arc GIS (2015). Features. http://www.arcgis.com/features/
11. Bassil, K.L., Shah, P.S., Shah, V., Ye, X.Y., Lee, S.K., Jefferies, A.L. (2014). Impact of Late Preterm and Early Term on Canadian Neonatal Intensive Care Units. Am J Perinatol. 31, 269-278
12. Binder, S., Hill, K., Meinzen-Derr, J., Greenberg, J.M., Narendran, V. (2011). Increasing VLBW Deliveries at Subspecailty Perinatal Centers via Perinatal Outreach. Pediatrics, 127(3), 487-493
13. Brown, S.A., Richards, M.E., Elwell, E.C., Rayburn, W.F. (2014). Geographic Information Systems for Mapping Maternal Ground Transport to Level III Care Neonatal Centers. Am J Perinatol, 31, 287-292
14. Canadian Institute for Health Information (2013). Patient Cost Estimators Methodological Notes and Glossary. https://www.cihi.ca/en/pce_methnotes_en.pdf
15. Chan K, Ohlsson A, Synnes A, Lee DS, Chien LY, Lee SK. Canadian Neonatal Network (2001). Survival, morbidity, and resource use of infants of 25 weeks' gestational age or less. Am J Obstet Gynecol, 185, 220–226

16. Chien, L., Whyte, R., Aziz, K., Thiessen, P., Matthew, D., Lee, S.K. (2001). Improved Outcome of Preterm Infants When Delivered in Tertiary Care Centers. Obstet Gynecol, 98(2)
17. Committee on Fetus and Newborn (2012). Levels of Neonatal Care. Pediatrics, 130(2), 587-597
18. Di Napoli, A., Di Lallo, D., Franco, F., Scapillati, M.E., Zocchetti, C., Agostino, R., Orzalesi, M. (2009) Access to Level III perinatal care for pregnancies of very short duration (<32 weeks). Perinatal Medicine. 37, 236-243
19. Faruque, L.I., Ayyalasomayajula, B., Pelletier, R., Klarenach, S., Hemmelgarn, B.R., Tonelli, M. (2012). Spatial analysis to locate new clinics for diabetic kidney patients in the underserved communities in Alberta. Nephrol Dial Transplant, 27, 4102-4109
20. Gilbert, W.M., Nesbitt, T.S. Danielsen, B. (2003). The Cost of Prematurity: Quantification by Gestatoinal Age and Birth Weight. Obstetricians & Gynecologists, 102(3)
21. Hakkinen, U., Iversen, T., Peltola, M., Seppala, T.T., Malmivaara, A., Belicza, E., Fattore, G., Numerato, D., Heijink, R., Medin, E., Rehnsberg, C. (2013). Health care performance comparison using a disease-based approach: The EuroHOPE project. Health Policy, 112, 100-109
22. Herrod, H.G., Chang, C.F., Steinberg, S.S. (2010). Variations in Costs for the Care of Low-Birth-Weight Infants Among Academic Hospitals. Clinc Pediatr, 49(5), 443-449
23. Hintz, S.R., Bann, C.M., Ambalavanan, N., Cotton, C.M., Das, A., Higgins, R.D. (2010). Predicting Time to Hospital Discharge for Extremely Preterm Infants. Pediatrics. 125(1).
24. Holmsgren, P.A., Hogberg, U. (2001). The very preterm infant - a population-based study. Acta Obstet Gynecol Scand, 80, 525-531
25. Isayama, T., Lee, S.K., Mori, R., Kusada, S., Fujimura, M., Ye, X.Y., Shah, P.S. (2012). Comparison of Mortality and Morbidity of Very Low Birth Weight Infants Between Canada and Japan. Pediatrics, 130(4), 957-965
26. Jochum, F., Schmidt, B., Schunk, K., Hesse, V., Distler, B., Laske, G., Moers, A., Dombrowsky, M. (2009). Quality of care of VLBW-neonates: relationship between unit volume and outcome is different between metropolitan and rural regions. Acta Paediatrica, 98, 609-612
27. Johnston, K.M., Gooch, K., Korol, E., Vo, P., Eyawo, O, Bradt, P., Levy, A., (2014). The economic burden of prematurity in Canada. BMC Pediatrics. 14(93).
28. Kitsommart, R., Janes, M., Mahajan, V., Rahman, A., Seidlitz, W., Wilson, J., Paes, B. (2009). Outcomes of Late-Preterm Infants: A Retrospective, Single-Center, Canadian Study. Clinical Pediatrics, 48(8), 844-850

29. Korvenranta, e., Linna, M., Hakkinen, U., Peltola, M., Andersson, S., Gissler, M., Hallman, M., Korvenranta, H., Leipala, J., Rautava, L., Tammela, O., Lehtonen, L. (2007). Differences in the length of initial hospital stay in very preterm infants. Acta Pediatrica, 96, 1416-1420
30. Korvenranta, E., Linna, M., Rautava, L., Andersson, S., Gissler, M., Hallman, M. Hakkinen, U., Leipala, J., Peltola, M., Tammela, O., Lehtonen, L. (2010). Hospital Costs and Quality of Life During 4 Years After Very Preterm Birth. Arch Pediatr Adolesc Med, 164(7), 657-663
31. Kramer, M.S., Platt, R.W., Wen, S.W., Joseph, K.S., Allen, A., Abrahamowicz, M., Blondel, B., Breart, G. (2001). A New and Improved Population-Based Canadian Reference for Birth Weight for Gestational Age. Pediatrics, 108(2)
32. Kuo, S., Kimata, C., Akamine, K., Young, B., Balaraman, B. (2012). Outcomes of inborn and transported extremely premature very-low-birthweight infants in Hawai'i. Pediatrics International, 54, 365-369
33. Laswell, S.M., barfield, W.D., Rochat, R.W., Blackmon, L. (2010). Perinatal Reginoalization for Very Low-Birth-Weight and Very Preterm Infants. JAMA, 304(9), 992-1000
34. Lehtonen, L.L., Rautava, L., Korvenranta, E., Korvenranta, H., Peltola, M., Hakkinen, U (2011). PERFECT preterm infant study. Ann Med. 43, 47-53
35. Manktelow, B.N., Seaton, S.E., Field, D.J., Draper, E.S. (2013). Population-Based Estimates of in-Unit Survival for Very Preterm Infants. Pediatrics, 131(2), 425-432
36. Howson, C.P., Kinney, M.V., Lawn, J.E. (2012). Born Too Soon: The Global Action Report on Preterm Birth. World Health Organization, March of Dimes.
37. Numerato, D., Fattore, G., Tediosi, F., Zanini, R., Peltola, M., Banks, H., Mihalicza, P., Lehtonen, L., Svereus, S., Heijink, R., Klitkou S.T., Fletcher, E., van der Heijden, A., Lundberg, F., Over, E., Hakkinen, U., Seppala, T.T. (2015). Mortality and Length of Stay of Very Low Birth Weight and Very Preterm Infants: A EuroHOPE study. American Academy of Pediatrics.
38. Peltola, M., Juntunen, M., Hakkinene, U., Rosenqvist, G. Seppala, T.T., Sund, R. (2011). A methodological approach for register-based evaluation of cost and outcomes in health care. Annals of Medicine, 43(1), S4-S13
39. Peters K.L. Rosychuk, R.J., Hendson, L., Cote, J.J., McPherson, C., Tyebkhan, J.M. (2009). Improvements of Short- and Long-Term Outcomes for Very Low Birth Weight Infants: Edmonton NIDCAP Trial. Pediatrics, 124(4), 1009-1020

40. Phibbs, C.S., Baker, L.C., Caughey, A.B., Danielsen, B., Schmitt, S.K., Phibbs, R.H. (2007). Level and Volume of Neonatal Intensive Care and Mortality in Very-Low-Birth-Weight Infants. N Engl J Med, 356, 2165-2175.
41. Public Health Agency of Canada (2004). Birth Weight for Gestational Age. Retrieved from: http://www.phac-aspc.gc.ca/rhs-ssg/bwga-pnag/index-eng.php
42. Qui, X., Lee, S.K., Tan, K., Piedboeuf, B. Canning, R. (2008). Comparison of Singleton and Multiple-Birth Outcomes of Infants Born at or Before 32 Weeks of Gestation. Obstet Gynecol, 111(2), 365-371
43. Qui, X., Lodha, A., Shah, P.S., Sankaran, K., Seshia, M.K., Yee, W., Jefferies, A., Lee, S.K (2012). Neonatal Outcomes of Small for Gestational Age Preterm Infants in Canada. Am J Perinatol. 29, 87-94
44. Ragowski, J.A., Horbar, J.D., Staiger, D.O., Kenny, M., Carpenter, J., Geppert, J. (2004). Indirect vs Direct Hospital Quality Indicators for Very Low-Birth-Weight Infants. JAMA, 291, 202-209
45. Rashidian, A., Omidvari A.H., Vali, Y., Mortaz, S., Yousefi-Nooraie, R., Jafari, M., Bhutta, Z.A. (2014). The effectiveness of regionalization of perinatal care services – a systematic review. Public Health, 128, 872-885
46. Rautava, L., Eskelinen, J., Hakkinen, U., Lehtonen, L. (2013). 5-Year Morbidity Among Very Preterm Infants in Relation to Level of Hospital Care. JAMA Pediatr, 167(1), 40-46
47. Rautava, L., Lehtonen, L, Peltola, M., Korvenranta, E., Korvenranta, H., Linna, M., Hallman, M., Andersson, S., Gissler, M., Lelpala, J., Tammela, O., Hakkinen, U. (2007). The Effect of Birth in Secondary- or Tertiary-Level Hospitals in Finland on Mortality in Very Preterm Infants: A Birth-Register Study. Pediatrics, 119(1), 257-263
48. Reugger, C., Hegglin, M., Adams, M., Bucher, H.U. (2012). Population based trends in mortality, morbidity and treatment for very preterm- and very low birth weight infants over 12 years. BMC Pediatrics, 12(17)
49. Rogowski, J.A., Horbar, J.D., Staiger, D.O. Kenny, M., Carpenter, J, Geppert, J. (2004). Indirect vs Direct Hospital Quality Indicators for Very Low-Birth-Weight Infants. JAMA, 291(2).
50. Russell, R.B., Green, N.S., Steiner, C.A., Meikle, S., Howse, J.L., Poschman, K. Dis, T., Potelz, L., Davidoff, M.J. Damus, K., Petrini, J.R. (2007). Cost of Hospitalization for Preterm and Low Birth Weight Infants in the United States. Pediatrics, 120(1)

51. Shah, P.S., Sankaran, K., Aziz, K. Allen, A.C., Seshia, M., Ohlsson, A., Lee, S.K. (2012). Outcomes of preterm infants <29 weeks gestation over 10-year period in Canada: a cause for concern? Journal of Perinatology, 32, 132-138
52. Soilly, A.L., Lejeune, C., Quantin, C., Bejean, S., Gouyon, J.B. (2014). Economic analysis of the costs associated with prematurity from a literature review. Public Health, 128, 43-62
53. St. John, E.B., Nelson, K.G., Cliver, S.P., Bishnoi, R.R., Goldenberg, R.L. (2000). Cost of neonatal care according to gestational age at birth and survival status. J Obstet Gynecol, 192, 170-175
54. Statistics Canada (2010). Road Network File – 2010 – Alberta. Retrieved from: http://data.gc.ca/data/en/dataset/0de78037-27c3-4844-b8f1-f9b70ea16b48.
55. Thompson, L.M., Armfield, N.R., Slater, A., Mattke, C., Foster, M., Smith, A.C. (2013). The availability, spatial accessibility, service utilisation and retrieval cost of paediatric intensive care services for children in rural, regional and remote Queensland: study proposal. BMC Health Services, 13(163)
56. Warner, B., Musial, M.J., Chenier, T., Donovan, E. (2004). The Effect of Birth Hospital Type on the Outcome of Very Low Birth Weight Infants. Pediatrics, 113(1), 35-41
57. Watson, S.I, Arulampalam, W., Petrou, S., Marlow, N., Morgan, A.S., Draper, E.S., Santhakumaran, S., Modi, N. (2014). The effects of designation and volume of neonatal care on mortality and morbidity outcomes of very preterm infants in England: retrospective population-based cohort study. BMJ Open, doi:10.1136/bmjopen-2014-004856
58. World Health Organization (2012). Six successes in making pregnancy safer. Retrieved from: http://www.euro.who.int/; 2010.
59. Xiangming, Q., Lodha, A., Shah, P.S., Sankaran, K., Seshia, M.K., Yee, W., Jefferies, A., Lee, S.K. (2012) Neonatal Outcomes of Small for Gestational Age Preterm Infants in Canada. AM J Perinatol. 29(2), 87-94.
60. Zupancic, J.A., Richardson, D.K., O'Brien, B.J., Schmidt, B., Weinstein, M.C. (2003). Daily Cost Prediction Model in Neonatal Intensive Care. International Journal of Technology Assessment in Health Care, 19(2), 330-338

7 Appendices

Appendix 7.1: Exclusion Criteria for Lethal Congenital Malformations

Malformation	ICD-10*
Anencephaly	Q00.0
Transposition of great vessels & Taussig-Bing syndrome	Q20.1
Hypoplastic left heart syndrome	Q23.4
Renal agenesis and dysgenesis	Q60.2
Anomalies of Diaphragm	Q79.0, Q79.1
Edwards syndrome	Q91.3
Patau syndrome	Q91.7

*International Classification of Diseases, Tenth Revision

Appendix 7.2: Levels of Neonatal Care [8]

Level of Care	Capabilities	Provider Types
Level I: Well newborn nursery	• Provides neonatal resuscitation at every delivery • Evaluate and provide postnatal care to stable term newborn infants • Stabilize and provide care for infants born 35-37 wk gestation who remain physiologically stable • Stabilize newborn infants who are ill and those born at <35 wk gestation until transfer to a higher level of care	Pediatricians, family physicians, nurse practitioners, and other advanced practise registered nurses
Level II: Special care nursery	Level I capabilities plus: • Provide care for infants born ≥32 wks gestation and weighing ≥ 1500g who have physiologic immaturity or who are moderately ill with problems that are expected to resolve rapidly and are not anticipated to need subspecialty services on an urgent basis • Provide care for infants convalescing after intensive care • Provide mechanical ventilation for brief duration (<24 h) or continuous positive airway pressure or both • Stabilize infants born before 32 wk gestation and weighing less than 1500g until transfer to a neonatal intensive care facility	Level I health care providers plus: Pediatric hospitalists, neonatologist, and neonatal nurse practitioners
Level III: NICU	Level II capabilities plus: • Provide sustained life support • Provide comprehensive care for infants born <32 wks gestation and weighing <1500g and infants born at all gestational ages and birth weights with critical illness • Provide prompt and readily available access to a full range of pediatric medical subspecialists, pediatric surgical specialists, pediatric anesthesiologists, and pediatric ophthalmologists • Provide a full range of respiratory support that may include conventional and/or high-frequency ventilation and inhaled nitric oxide • Perform advanced imaging, with interpretation on an urgent basis, including computed tomography, MRI, and echocardiography	Level II health care providers plus: Pediatric medical subspecialists, pediatric anesthesiologists, pediatric surgeons, and pediatric ophthalmologists

Appendix 7.3: Complete study dataset variables listed by data origin

Alberta Health Services - Alberta Perinatal Health Program

Field Name	Description
A11	Hypertension 140/90 or greater as rec. on antepartum risk assess
A12	Antihypertensive drugs as recorded on antepartum risk
ABORTIONS	Tot # of pregnancy losses prior to 20 wks gestation or < 500 gms, incl. ectopic pregnancy. Includes both therapeutic & spontaneous abortions (S. AB did not collect until 2007/2008 - but parity avail)
APGAR1	Apgar score assessed at 1 minute
APGAR5	APGAR score assessed at 5 minutes after delivery
APGAR10	Apgar score assessed at 10 min. (usu blank if 5 min APGAR is 7+)
B06	Small for dates as recorded on antepartum risk assessment in Past Obstetrical History
BIRTH_EVENT_ID	Unique Identifier for a birth event assigned by APHP
BIRTH_ORDER	Sequence the baby was born, (1), (2) etc. Combined with the birth event ID to uniquely identify a new born
BIRTH_WEIGHT	First weight of newborn after birth, in grams.
C11	Gestational diabetes documented as rec. on antepart. risk assess
C15	Poor weight gain (26 36 weeks < 0.5 kg/week or weight loss)
C16	Smoker anytime during pregnancy
CESAREAN_BIRTH_TOTAL	Previous total # of Cesarean Birth excluding current cesarean birth
CONGENITAL_ANOMALY	Indicates the presence of a fetal anomaly
D03	Alcohol > 3 drinks on any one occasion during pregnancy.
D04	Alcohol > 1 drink per day throughout pregnancy
D05	Drug dependent, inappropriate or excessive use of any substancewhich may adversely affect the outcome of the pregnancy
DM_BRCH	Vaginal Breech Delivery (will include DM_BS, DM_BA, BM_BE)
DM_CS	Cesarean Section
DM_FRCP	Vaginal delivery with forceps
DM_SPV	Spontaneous Vaginal

DM_UKN	Unknown method of delivery
DM_VACM	Vaginal delivery with vacuum
DOD	Month & year of Newborn date of death
DURATION_OF_LABOUR_HRS	Total hours of labour
DURATION_OF_LABOUR_MIN	Total minutes of labour
FISC_YR	Fiscal year of the date of birth
GENDER	Gender of the baby
GESTATIONAL_AGE_AT_DELIVERY	Gestational age at delivery (continuous number)
GRAVIDA	The number of pregnancies including the current birth that a woman has had regardless of gestation or outcome (S. AB did not collect until 2007/2008 - but parity avail)
ID	APHP ID
IN_AH_RGST_CHLD	Indicates (Y/N) whether maternal PHN found in AH Registry
IN_AH_RGST_MOM	Indicates (Y/N) whether newborn ULI found in AH Rgst (04/05 on)
IR_IUGR	Suspect intrauterine growth restriction (IUGR) as indic. for induction
IR_PIH	Pregnancy induced hypertension (PIH) rec. as indic. for induction
IR_PRM	Premature rupture of membranes rec. as indication for induction
LIVING	Tot # of children currently living that were born to this woman excl. this birth (S. AB did not collect until 2007/2008 - but parity avail)
MAT_GHD	Geographical hospital district (Clinical Catchment Area)
MAT_RHA	Health region or zone of residence
MATERNAL_AGE	Mother's age at delivery
MATERNAL_DATE_OF_BIRTH	Month & year of Maternal date of birth
MATERNAL_PHN_ASN	Scrambled Maternal PHN
MATERNAL_POSTAL_CODE	Maternal Postal Code
MDE_DOD	Month & year of maternal date of death
MDE_GAD	Number of completed wks of pregnancy at time of maternal death
NEO_DEATH	The post outcome of a live birth. Early - up to 7 days. Late - 7 up to
NEWBORN_BIRTH_DATE	Month & year of Newborn date of birth
NEWBORN_ULI_ASN	Scrambled Baby ULI
NICU_ADMISSION	Baby admitted to NICU or SCN
OD_EPCD	Elective primary cesarean section - breech or transverse lie
OD_ERCS	Operative delivery for ??

OD_FHR	Operative delivery for fetal heart rate abnormalities
OD_MULTIP	Operative delivery for multiple pregnancy
OD_PPREIA	Operative delivery for placenta previa
PARITY	Total number of previous pregnancies
PREGNANCY_OC	The outcome of delivery for each baby born
PREGNANCY_TYPE	Identifies pregnancy type i.e: single / multiple gestation
PRETERM	Tot # of babies born to this woman btwn 20 and <37 comp wks gestn excl curr birth (S. AB didn't collect until 2007/08 - but pty avl)
RI_BM	Resuscitative intervention: Bag/Mask -Pos. pressure ventilation
RI_CPR	Resuscitative intervention: Cardio Pulmonary Resuscitation
RI_ETM	Resuscitative intervention: Endo-tracheal Tube - Meconium
RI_ETPPV	Resuscitative intervention: Endo-tracheal Tube - Pos. Press Vent
RI_MEDS	Resuscitative intervention: Medication given for resuscit. of infant
RI_NONE	No interventions
RI_OXY	Resuscitative intervention: Free flow oxygen admin.cto infant; Started coding for S. perinatal in phases through 2007. Calg hosps started collect April 1, 2009 (do not use prior to 2007 for AB & 2009 for Calg)
RI_SUC	Resuscitative intervention: Suction administered to infant; Started coding for S. perinatal in phases through 2007. Calg hosps started collect April 1, 2009 (do not use prior to 2007 for AB & 2009 for Calg)
TERM	Tot # of babies born to this woman at >= 37 comp wks gestn excl current birth (S. AB did not collect until 2007/2008 - but parity avail)
TOTAL_ANTEPARTUM_RISK_SCORE	The total antepartum risk score from the delivery record part one
TOTAL_INTRAPARTUM_RISK_SCORE	The total intrapartum risk score from the delivery record part one
TRIAL_OF_LABOUR_AFTER_PREVIOUS_C_TYPE _OF_LABOUR	Indicates the woman had a previous C-section and has been allowed a trial of labour with the intent to deliver vaginally

Alberta Health - Population Registry

Field Name	Description
FISC_YR	Fiscal Year of registration
LOCTN_HRGN_CODE_FYE	Registrant Regional Health Authority derived from postal code at fiscal year-end. Derivation: Derived from the Postal Code location of the registrant at the end of the fiscal year using April 98 boundaries
NEWBORN_ULI_ASN	Recipient anonymous unique identifier
PERS_ACTV_COVRG_IND_FYE	A flag that indicates whether or not a registrant is active at the end of the fiscal year. Valid values: 1 =active; 0 = not active
PERS_GENDER_CODE_MC	A code depicting the biological sex of Registrant Instance: 0 Derivation: Direct copy from the Registration Dependant Interface File.
PERS_SOCIO_ECON_STATUS	Registrant alternate premium arrangement (Socio-Economic Status) code Valid Values: A Aboriginal Group, W Welfare, S Government Sponsored Programs, O All other remaining records
RCPT_LOCTN_FSA	First three letters of recipient postal code
RCPT_BIRTH_YEAR	Recipient Year of Birth
RCPT_BAND_FLAG	Indicates whether the recipient is a member of a Native Band

Alberta Health - Inpatient File (DAD)

Field Name	Description
HLTH_DX_CODE_MR	Diagnosis, condition, or problem - the reason for the service being provided - most responsible
HLTH_DX_CODE_OTH2-25	Diagnosis, condition, or problem - the reason for the service being provided - other reasons
HLTH_DX_PFX_CODE_MR	A character to further distinguish an ICD-10-CA code (most responsible diagnosis)
HLTH_DX_PFX_CODE_OTH_2-25	A character to further distinguish an ICD-10-CA code (other diagnoses)
HLTH_DX_TYPE_CODE_MR	Alpha or numeric code used to further describes the most responsible diagnosis
HLTH_DX_TPE_CODE_OTH_2-25	Alpha or numeric code used to further describes the other diagnoses
PERS_GENDER_CODE_MC	Biological sex of the recipient at time of service
REC_SUBM_FAC_ID	Submitting institution identifier in format Prov#, Level of Care, Unique Fac #
SE_INTRV_CODE_PR	Operative or non-operative intervention performed on the patient - primary procedure

SE_INTRV_CODE_2-20	Operative or non-operative intervention performed on the patient - other procedure
SE_INTRV_START_DATE_PR	Date on which a reported intervention was performed - primary procedure (1800-01-01 for invalid)
SE_INTRV_START_DATE_2-20	Date on which a reported intervention was performed - other procedure (1800-01-01 for invalid)
SEPI_CMG_CODE	Case Mix Group - grouper used to create homogenous patient clusters
SEPI_CPLX_LVL_CODE_CIHI	Used to determine funding allocation - data is derived by Alberta or CIHI as part of the grouper process
SEPI_DISCH_DISPO_CODE	Location where the patient was discharged or the status of the patient on discharge
SEPI_END_DATE	Calendar date (YYYYMMDD) when patient was formally discharged
SEPI_GRPR_DESC	The complete description of the grouper methodology used to group the inpatient or ambulatory care data
SEPI_RIW_VALUE	Resource Intensity Weight - expected relation of costs between patient types (1.0000 = avg cost)
SEPI_SPEC_CARE_ADMIT_UNIT_CODE_1-3	Identifies the type of special care unit where the patient receives critical care
SEPI_START_DATE	Calendar date (YYYYMMDD) that patient officially registered as recipient (newborn=DOB)
FISC_YR	Fiscal Year of inpatient separation
NEWBORN_ULI_ASN	Recipient Anonymous Unique Identifier; based on Rcpt_PHN (2002/03-2009/10 and Stkh_Rcpt_PHN_Mc (1999/00-2001/02)
SEPI_SCU_DURA_DAYS_1-3	Length of stay, in days, in a special care unit; Less than 24 hours is recorded as one day; pre-2002/03=Sepi_SCU_Dura_Days_1-3; 2002/03 forward = Sepi_Spec_Care_Disch_Dt - Sepi_Spec_Care_Admit_Dt

Vital Statistics Death Registry

Field Name	Description
DETHDATE	Date of Death recorded on medical certificate of death
NEWBORN_ULI_ASN	Recipient anonymous unique identifier
U_CAUSE	A 5-digit mortality code based on the International Classification of Diseases - Cause of Death

	Codes. From 1983 to 1999, the 9th revision was used and from 2000 to present, the 10th revision. For records using ICD-9, all codes between 800x-999x are E-codes (the 'E' has not been entered).

Postal Code Dataset

Field Name	Description
PC_MUNICIPAL_NAME	Municipality name
PC_PEER_GROUP	Alternative classification for each postal code zone with relation to location and population proximity
PC_POP_PROXIMITY	Categorical classification of proximity to city centres
PC_POP_SIZE	Estimated number of individuals living in postal code area
PC_POSTAL_CODE	Postal code
PC_ZONE_NAME	Health zone postal code resides in

Distance Dataset

Field Name	Description
L_HOSPITAL	NICU Hospital 3 letter abbreviation
L_LENGTH_METERS	Driving distance in meters from home address to hospital
L_LENGTH_KM	Driving distance in kilometers from home address to hospital
L_Merge _Dist_1	Original merge with all distances to a NICU. Provided distances from maternal address to NICU hospital infant was admitted too
L_Merge_Dist_2	Secondary merge of those admissions not to a NICU. Identifies the infants nearest distance to a NICU (they did not seek treatment at).
PC_LONGITUDE	Postal code longitude coordinates
PC_LATITUDE	Postal code latitude coordinates
MATERNAL_POSTAL_CODE	Maternal postal code

CIHI Costing Database

Field Name	Description
C_COST_STANDARD_HOSPITAL_STAY	Cost per standard hospital stay (hospital specific)
C_HOSPITAL_NAME	Hospital name
C_REGIONAL_STANDARD_USED	Yes/No indicator for if the health zone average was used in cases where a hospital specific cost per standard hospital stay was not available
REC_SUBM_FAC_ID	Hospital identifier code

Derived Variables

Field Name	Description
BW500	Birth weight less than or equal to 500g (Indicator variable)
BW_TAB	Birthweight classifications (categorical variable)
C_STAY_COST	Hospital cost (Cost per standard hospital stay multiplied by the RIW value)
C_TOTAL_NEWBORN_COST	Newborn total hospital cost over study period
C_YEAR	Total hospital cost for very preterm infant after a year since birth
CUTOFF_LGA	Cut-off variable for LGA variable
CUTOFF_SGA	Cut-off variable for SGA variable
D365_ANEM_PREM	Anemia of prematurity indicator variable (P612)
D365_BRONC_DYS	Bronchopulmonary dysplasia indicator variable (P271)
D365_INTRA_HEM	Intraventricular hemorrhage indicator variable (P52*)
D365_NECRO_ENTER	Necrotizing enterocolitis indicator variable (P77*)
D365_NEO_JAUN	Neonatal jaundice indicator variable (P590)
D365_OTH_RESP_PROB	Other respiratory problems after birth indicator variable (P28*)
D365_PER_DUC_ART	Persisting ductus arteriosus indicator variable (Q250)
D365_RESP_DIS_SYN	Respiratory distress syndrome indicator variable (P22*)
D365_RETIN_PREM	Retinopathy of prematurity indicator variable (H351)
D365_YEAR_SINCE_BIRTH	Time variable indicating a year since infant's birth
D_MALFO	Any malformations indicator variable (Q0* - Q8*)
DAYS_UNTIL_DEATH	Time variable indicating days until infant death
DUP	Reference variable providing a numeric order to multiple inpatient records from the same infant
DUP_GROUP_TOTAL	Lists number of occurrences of a reoccurring inpatient record
EPISODE	Variable used for HEPLOS calculation; indicates an episode continues if the discharge and admission are on the same day or one day apart
FLOS	First hospitalization length of stay (including transfers)
FLOS_PERIODS	FLOS variable in categorical periods (<=1 day, 2-3 days, 4-7 days, 7-30 days, >30 days)
FIRST	Reference variable indicating the first inpatient record of multiple hospitalizations records

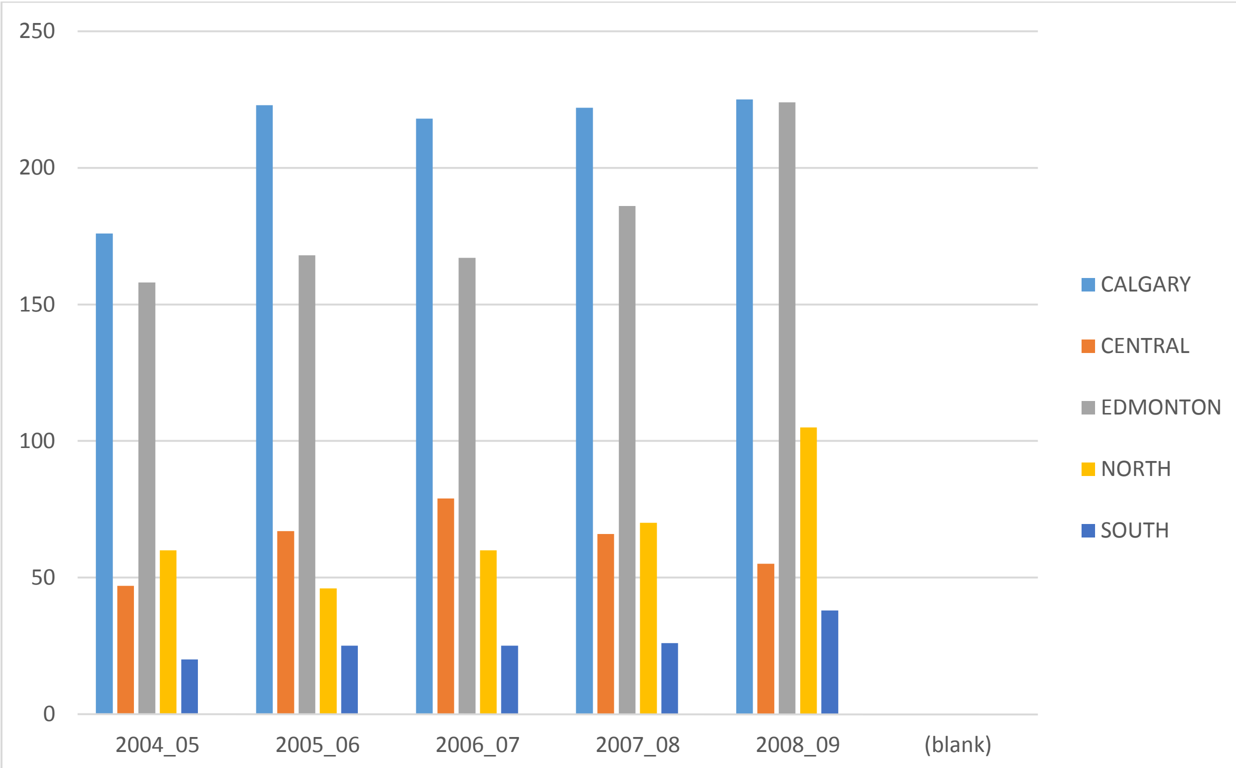
FIRSTHOSP_DEATH	Indicator variable for if death occurred during first hospitalization
FIRST_DELIVERY	Indicator variable for if the infant's birth was the mother's first delivery
FIRST_NICU_ADMIT	Variable identifying if the record was the first NICU admittance using APHP's variable "nicu_admission"
GA22_29	Indicator variable for if gestational age is between 22-29
GA31_32	Indicator variable for if gestational age is between 31-32
GA_SCALE	Categorical variable indicating if infant is small for GA, normal for GA, or large for GA
GEST_TAB	Categorical grouping of gestational ages
HEPLOS	Hospital episode length of stay (including transfers)
IOC_ART_CATH	Indicator of care – Artherial catheterization
IOC_CPAP	Indicator of care – Continuous positive airway pressure
IOC_CARD_RESUS	Indicator of care – Cardiopulmonary resuscitation
IOC_ENDOTRACH_TUBE	Indicator of care – Insertion of endotracheal tube
IOC_MUSC_REPAIR	Indicator of care – Repair muscles (inguinal hernia)
IOC_PARENT_INFUS_NUTR	Indicator of care – Parenteral infusion of concentrated nutritional substances
IOC_RES_IMAG_BRAIN	Indicator of care – Magnetic resonance imagining of brain and brain stem
IOC_TOMO_HEAD	Indicator of care – Computerized axial tomography of head
IOC_ULTRA_HEAD_NECK	Indicator of care – Diagnostic ultrasound of head and neck
IOC_ULTRA_HEART	Indicator of care – Diagnostic ultrasound of heart
IOC_UMB_V_CATH	Indicator of care – Umbilical vein catheterization
IOC_VEN_CATH	Indicator of care – Venous catheterization
INDEX_MONTH	Month of hospital admission
INDEX_WEEKDAY	Weekday of hospital admission
INFANT_BIRTH_YEAR	Infant year of birth
LOS	Length of stay for patient record (not including transfers)
LOS30	30 day length of stay
LOS365	Year length of stay
LOS90	90 day length of stay
LEVEL_1TO2_NICU	Admission into a Level 1-2 NICU Hospital
LEVEL_1TO3_NICU	Admission into a level 1-3 NICU Hospital
LGA	Large for gestational age
MALE	Indicator for male sex of infant
MULTIPLE_BIRTH	Indicator for multiple births in pregnancy

NICU_ADMIT	NICU admission as indicated by sepi_spec_care_admit_unit variable
NGA	Normal size for gestational age
NINETY_DAY_MORTALITY	Indicator for if death occurred within 90 days of birth
OBSTETRIC_LEVEL	Obstetric level of admitting hospital (Rank 0-3)
RESUSITATION	Indicator variable if any form of resuscitation is used (as coded by the APHP)
SEVEN_DAY_MORTALITY	Indicator for if death occurred within 7 days of birth
SGA	Small for gestational age
TEACH_HOSP	Admission into a teaching hospital
THIRTY_DAY_MORTALITY	Indicator for if death occurred within 30 days of birth
TIME_TO_DEATH_SINCE_DISCHARGE	Time variable for time till death after discharge (death date – admission discharge)
TRANSFER_HIGHLOW	Transfer from a high level obstetric hospital to a low level obstetric hospital
TRANSFER_LOWHIGH	Transfer from a low level obstetric hospital to a high level obstetric hospital
TRANSFER_TO_LEV3	Transfer to a level 3 obstetric hospital
VLBW_BABY	Very low birth weight baby indicator
VLGA_BABY	Very low gestational age baby indicator
TRANSFER	Indicator for if an infant was later transferred during the present admission
YEAR_MORTALITY	Indicator for if death occurred within 1 year of birth

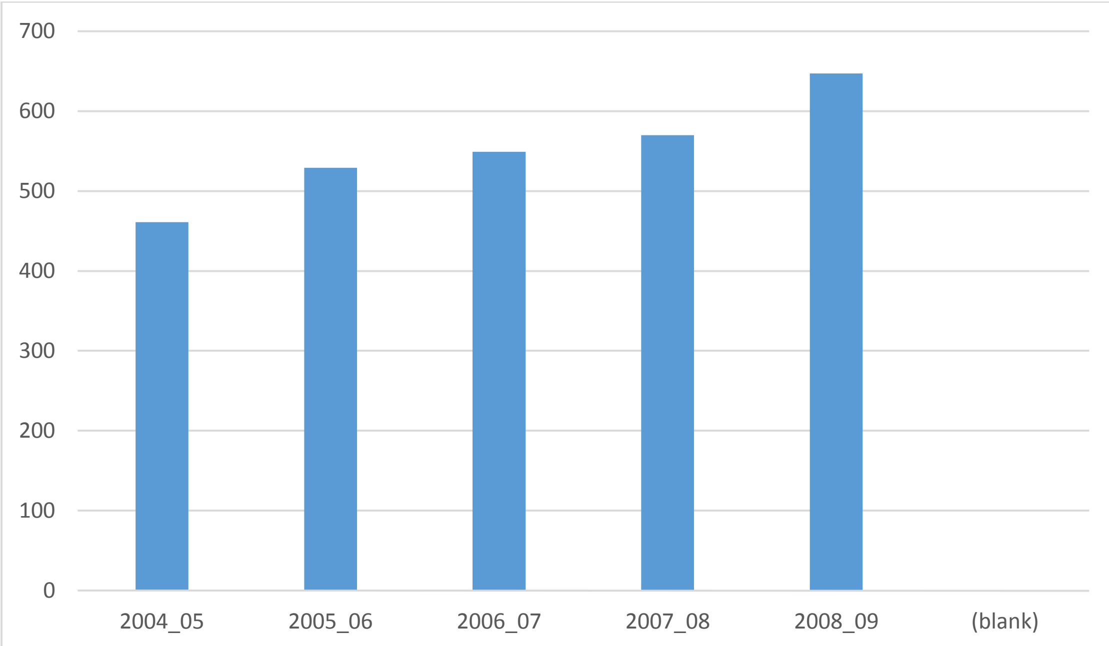
Appendix 7.4: Neonatal Intensive Care Unit Level 2 & 3 Hospitals in Alberta

Hospital name	Hospital ID	NICU Level	# of Beds (2015)	Facility ID	Latitude Coordinate	Longitude Coordinate
Royal Alexandra Hospital	RAH	3	69	80043	53.556973	-113.496645
Stollery Childrens Hospital	SCH	3	18	80044	51.074980	-114.148571
Foothills Medical Centre	FMC	3	36	80016	51.06563	-114.131862
Grey Nuns Hospital	GNH	2	29	80042	53.462511	-113.429334
Misericordia Community Hospital	MCH	2	12	80041	53.520348	-113.612561
Red Deer Regional Hospital	RDH	2	11	80092	52.260727	-113.817527
Queen Elizabeth II Hospital	QEH	2	8	80056	55.175301	-118.786557
Peter Lougheed Centre	PLC	2	28	80148	51.078848	-113.983977
Rockyview General Hospital	RGH	2	24	80020	50.989968	-114.096553
Medicine Hat Regional Hospital	MHH	2	3	80079	50.034646	-110.702264
Chinook Regional Hospital	CRH	2	11	80071	49.685215	-112.815109

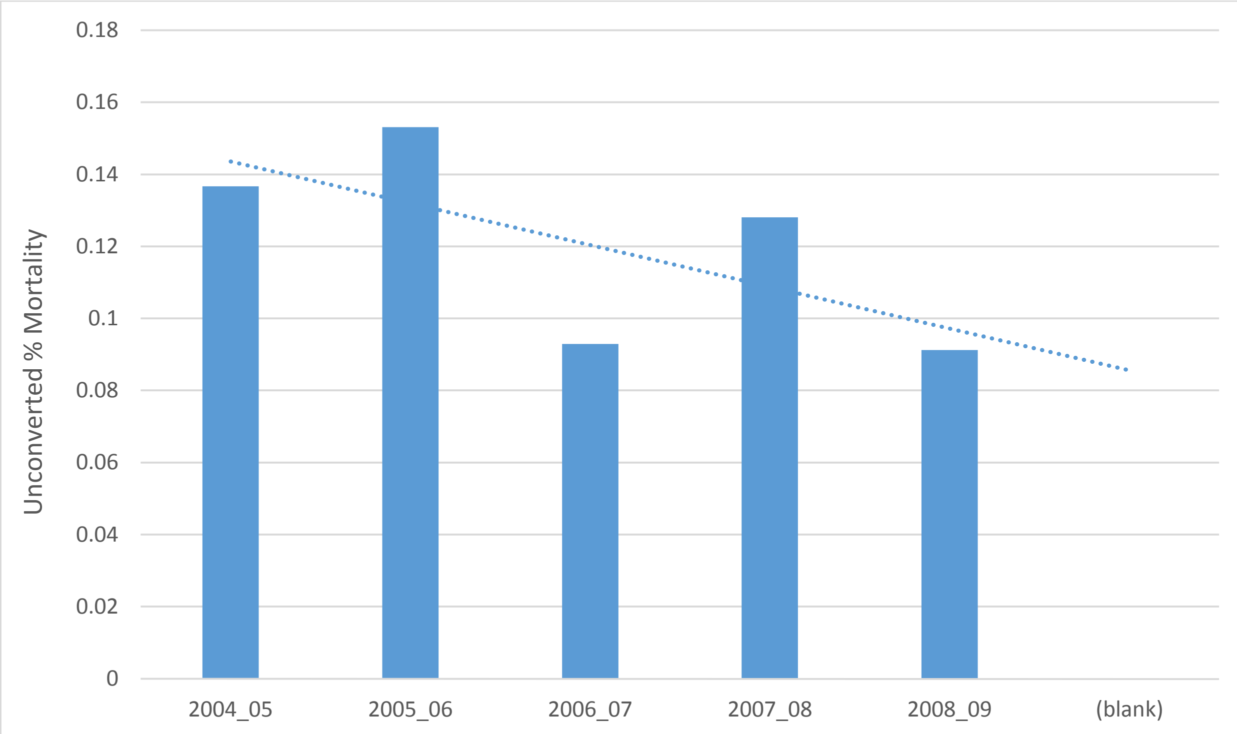
Appendix 7.5: Number of very preterm infants born in each health zone from 2004-2009



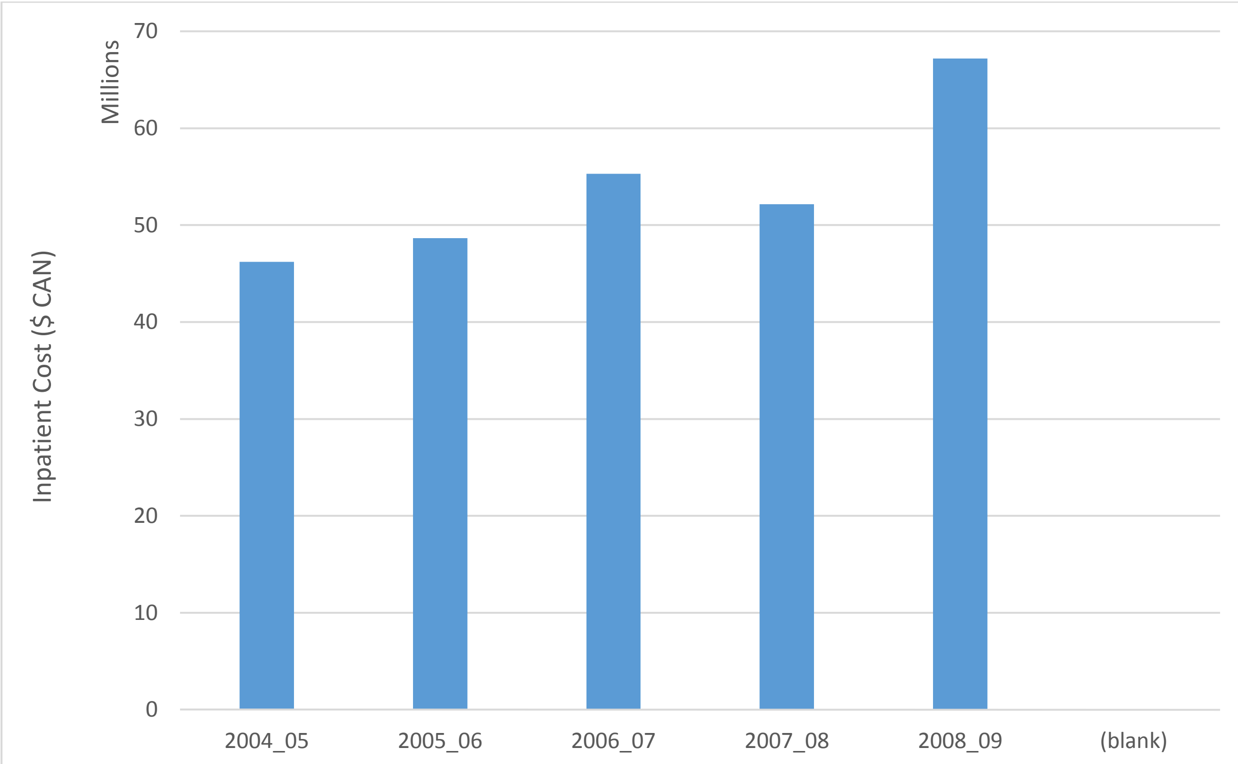
Appendix 7.6: Number of very preterm infants born in Alberta from 2004-2009



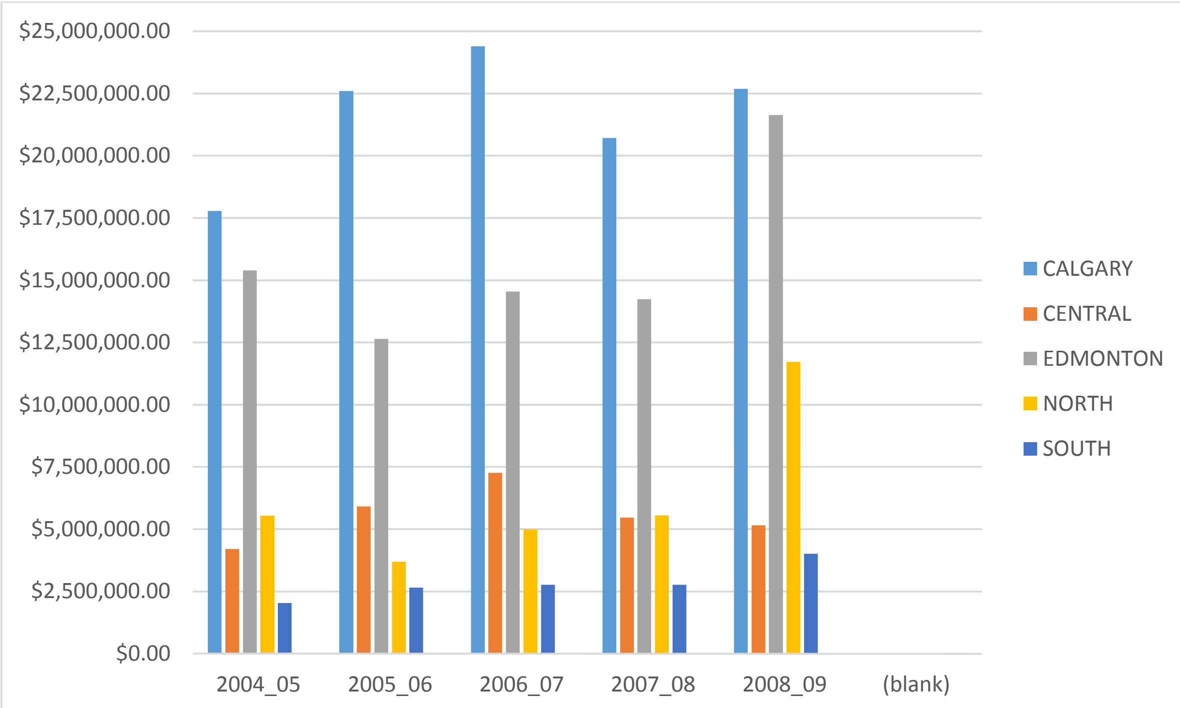
Appendix 7.7: Unconverted death rate of very preterm infants by fiscal year



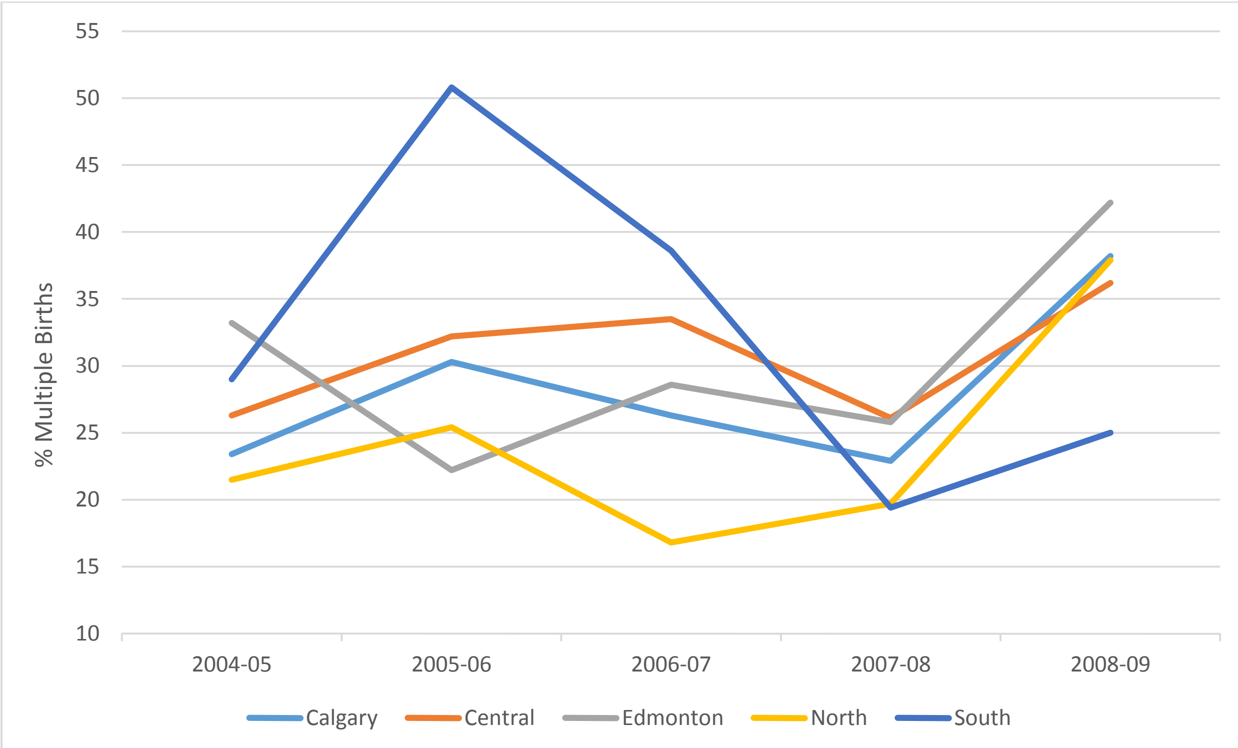
Appendix 7.8: Sum of total inpatient cost in very preterm infants by fiscal year



Appendix 7.9: Sum of Inpatient costs by fiscal year and health zone



Appendix 7.10: Percentage of VPI Infants that are Multiple Births by Health Zone and Fiscal Year



Appendix 7.11: Regression Coefficient Tables for Year Mortality and Hospital Episode LoS

	Year Mortality **Logistic Regression**		**Hospital Episode LoS** **Negative Binomial Regression**	
	Regression Coefficient	**Odds Ratio**	**Regression Coefficient**	**Incidence Rate Ratio**
Intercept	-2.87	-	3.13	-
Level 3 NICU	-0.61*	0.54	0.54**	1.72
GA 22-25	3.11**	22.31	0.18**	1.20
GA 26-28	1.33**	3.78	0.43**	1.53
Apgar 5 Score 1-5	1.81**	6.13	-0.39**	0.67
Small for GA	0.87**	2.39	-0.059	0.94
Transfer to Level 3 NICU	-0.87*	0.42	0.78**	2.18
Born in Calgary/Edmonton	-0.34*	0.71	0.026	1.03
Multiple Birth	-0.29	0.75	0.073*	1.07
First Delivery	-0.25	0.78	0.054	1.05
Malformation	-2.87	0.79	0.36**	1.43

** Statistically significant (P<0.05)*
*** Statistically significant (P<0.01)*