Early Life Environments and Long Term Outcomes

by

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Abstract

A large literature has linked "***in utero***" environment to health and socio-economic outcomes in adulthood. We consider the effect of early life environments on health and skill formation outcomes. We first evaluate the impact of perinatal-neonatal level of technology at birth, which varies across delivery institutions, on the long-term neurodevelopmental outcomes of children with Cerebral Palsy. The level of technology at delivery determines the type of therapy newborns receive immediately after birth. The type of therapy is critical to prevent or treat adverse events around labor and delivery which determine later neurological and neurocognitive impairments such as CP. We evaluate the relationship between availability of neonatal technology, which is associated with levels of care at delivery hospitals, and CP nonambulatory status, using data from the Canadian Multi-Regional Cerebral Palsy Registry. In a follow-up paper we further explore the efficiency of neonatal transfers across Quebec neonatal system. We find robust evidence that there is no statistical significant relationship between level of neonatal care at birth and CP severity. This finding means that differences in levels of neonatal care and associated technology available at delivery are not associated at the margin with the risk of a non-ambulatory CP phenotype among children with CP. Overall we conclude that, in the Quebec regionalized neonatal care system, there is no gain to increasing the level of care assigned to mothers at risk of CP.

We estimate the effect of mothers' participation in the Supplementary Nutrition Assistance Program and the Special Supplemental Nutrition Program for Women, Infants, and Children on early cognitive and non-cognitive developmental outcomes as measured by the Bayley Scales of Infant Development. Our data are from a large, prospective, community-based panel study of mother-infant pairs. In this rich data set we can directly identify the change in neurodevelopmental outcomes associated with changes in food programs uptake. In a model where unobserved heterogeneity only affects the level of neurodevelopmental outcomes this can be interpreted as a causal effect. Our results suggest that brief prenatal investments may be more cost effective than traditional educational interventions in improving early childhood developmental outcome.

Keywords: Economics of human development, capacities, maternal and fetal nutrition, neonatal health, "*in utero*" environment.

Dedication

To my dad and mom.

“Then you will know the truth, and the truth will set you free” John 8:32

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Chapter 1.

The impact of Level of Care at Birth on Long Term Health Outcomes: Evidence from Children with Cerebral Palsy

Introduction

The adoption and diffusion of new technological advances in fetal diagnostics and therapy has changed the way doctors deliver care to neonates in North America and around the world. These innovations have resulted in the ability to save lives of the majority of even the sickest and smallest newborns (23 to 25 weeks of gestational age), which thirty years ago were not considered viable. However, improvements in neonatal health outcomes have come at an increasing cost to health care systems. *Perinatal regionalization*, meaning the tiered provision of neonatal care, emerged over time as a strategy to balance this fundamental tradeoff and provide optimal, risk-appropriate maternal child services for a geographically dispersed population[1]. These systems of regional perinatal services are now common across North America and around the world, and are linked to improved outcomes for high-risk infants born either preterm or with serious medical or surgical conditions [2], [3].

Regionalization of perinatal care has facilitated the diffusion of newly-developed neonatal technologies and improved access of newborns in the community to innovative interventions. Evidence from existing clinical and health research links perinatal regionalization with improved neonatal outcomes for infants born preterm and with low birth weight [1]. The impact of improved neonatal interventions in early childhood on later life outcomes is documented in a growing economics literature. In particular, Bharadwaj et al. show that children who receive extra medical care at birth have lower mortality rates and higher test scores and better grades in school [4]. Moreover, the effects of

poor neonatal health on adult outcomes are set very early [5]. However, there are growing concerns about the high costs of neonatal intensive care as well as the substantial financial burden survivors of neonatal intensive care might pose on their families and health care system [6], [7]. While the overall efficacy of specific advances in neonatal-perinatal medicine has been established in the literature [8]–[10], limited evidence exists on the overall effectiveness of technological change in neonatal care and its impact on long-term health outcomes.

This study evaluates the impact of perinatal-neonatal level of technology, which varies across delivery institutions, on the long-term neurodevelopmental outcomes of children with Cerebral Palsy (CP). The level of technology at delivery determines the type of therapy newborns receive immediately after birth. The type of therapy is critical to prevent or treat adverse events around labor and delivery which determine later neurological and neurocognitive impairments such as CP[11]. Specifically, we evaluate the relationship between availability of neonatal technology, which is associated with levels of care at delivery hospitals, and CP non-ambulatory status, using data from the Canadian Multi-Regional Cerebral Palsy Registry (CCPR).

The challenge of examining this relationship is that the level of technology available at delivery is not randomly assigned. We aim to remove selection bias (confounding by indication) which originates as a result of high-risk pregnancies and births being assigned to hospitals with better levels of care and associated medical technology (levels II, III). To deal with this bias, we use controls for biological risk factors for CP. Additionally, we consider an instrumental variables strategy to deal with possible unobserved risk factors.

Our empirical approach relies upon propensity score-matching (PSM) and multivariate regression methods using high-quality observables. We motivate the selection on observables assumption because CCPR contains all known prenatal, neonatal and postnatal risk factors associated with CP. We have made use of all known causal and correlated risk factors associated with CP as reported in the medical literature, including selected maternal behaviours, such as drug addiction and smoking. However, there may be other, unknown causes of CP related to maternal behaviours

that are correlated with decisions regarding choice of delivery hospital. To account for these potential unknown factors, we use instrumental variables methods.

To preview our main results, we find robust evidence that there is no statistical significant relationship between level of neonatal care at birth and CP severity (non-ambulatory status). This finding means that differences in levels of neonatal care and associated technology available at delivery are not associated at the margin with the risk of a non-ambulatory CP phenotype among children with CP. We conclude that, in the Quebec regionalized neonatal care system, there is no gain to increasing the level of care assigned to mothers at risk of CP.

This paper makes three main important contributions to the economics and health services research literature which links advances in medical technology to improved health outcomes. First, we estimate the effect of neonatal-perinatal technology availability at delivery on long-term neurodevelopmental outcomes. Second, we use uniform definitions of level of care (consistent with the American Academy of Pediatrics standards) across the province of Quebec, Canada and what we believe is the best feasible case-mix adjustment (aka: good observed control variables) between the three groups of hospitals. Third, we are the first to study the effect of neonatal care-level and technology at delivery on long-term health outcomes using instrumental variables methods.

The paper proceeds as follows. Section 1 provides the background and an outline of our identification strategy using a potential outcomes framework. We also describe here our main regression model. Details regarding our data sources, sample inclusion, and exclusion criteria as well as relevant medical background, are provided in Section 2. Section 3 begins by outlining our empirical framework and details the estimation strategies. In this section we also report our main estimates and explore robustness of these results. We offer conclusions in Section 4.

1.1. Background

1.1.1. Cerebral Palsy (CP)

CP is a set of variable clinical symptoms which result from either an anomaly and/or early damage to the motor regions of the brain, causing graded levels of observable motor dysfunction [12]. CP remains the largest single cause of childhood physical disability in the developed world [13] and it is estimated to affect approximately 2.0-2.5 infants per 1,000 live births [14]. CP is believed to be caused by congenital brain abnormalities or acquired brain injuries [11]. However, little is known regarding the factors that determine the severity of CP and whether the level of neonatal care available at the site of birth might influence the eventual severity of the condition.

Although onset is at birth or in early childhood, CP persists throughout an individual's life and implies a significant economic burden. The US Center for Disease Control (CDC) and Prevention estimated the lifetime costs of CP per individual to be $921,000 in 2003, [15]. A more recent Danish study reports the approximate lifetime cost of CP was 860,000 Euros for men and 800,000 Euros for women. The largest component of these expenditures was social care costs, particularly during childhood [16]; however the lifetime costs of CP depend on the severity of the condition and specifically on non-ambulatory status.

The International CP Task Force recognized that some cases of CP probably originate in labour; however, it is now widely accepted that most CP cases are not the result of intrapartum events, and in particular of substantial intrapartum hypoxia [17]. However, allegations of causation of CP in obstetrical clinical negligence claims are common and usually focus on the obstetrical care provided in the intrapartum period [18], [19]. Past studies have explored the relation between the quality of care given to a mother during labour and delivery and later CP, and an association between suboptimal care and CP was found in only a small proportion of CP cases [20]. However, past research did not control for the level of immediate postnatal care available subsequent to labor and delivery. Moreover, the relationship between the level of neonatal care

available at birth, the severity of CP, and the impact of perinatal and neonatal factors on later severity is presently unknown.

1.1.2. Perinatal Regionalization

Following some initial recommendations for the regional development of maternal and perinatal health services made by the Committee on Perinatal Health (March of Dimes) in a 1976 report, the American Academy of Pediatrics (AAP) Committee on Fetus and Newborn issued two policy statements on levels of neonatal care [21], [22]. The 2012 policy statement recommended regionalized systems of perinatal care "to ensure that each newborn infant is delivered and cared for in a facility appropriate for his or her health care needs and to facilitate the achievement of optimal outcomes." (p. 1346).

In North America, the concept of perinatal regionalization emerged in North America, first in Canada [23], followed in the U.S. in 1971 by the American Medican Association's House of Delegates' report [24]. Delivery hospitals were classified into one of three levels according to the degree of complexity of maternal and perinatal care each was capable of providing. European countries had implemented decentralized maternity services as well to ensure good access to necessary care independent of place of residence [25].

A large body of clinical literature documents that high-risk infants have better health outcomes in deliveries with neonatal care (typically level II or III hospitals). In a comprehensive review of 41 published studies conducted between 1979 and 2008, involving the use of different research designs (including randomized, clinically-controlled trials, cohort, and case-control studies), Lasswell in [1] conclude: "for VLBW (birth weight <1,500 g) and VPT [very preterm] (less than 32 weeks' gestation) infants, birth outside of a level III hospital is significantly associated with increased likelihood of neonatal or predischarge death." However, more recent economics literature has linked neonatal care to longer-term outcomes, including educational achievement and long-term health status.

Due to its size and relatively sparse population, Canada has a highly regionalized neonatal-perinatal care system and nearly all deliveries take place in public hospitals[26]. Low-risk deliveries are carried out at level I facilities (well newborn nurseries), while medium and high-risk deliveries are referred to level II (specialty care) or level III (subspecialty care) hospitals, according to hospitals' catchment areas. This classification reflects differences in the level of perinatal resources and obstetric competence available at a specific delivery hospital.

High risk deliveries are identified based on unified national medical guidelines [27], [28] and are referred to central or regional hospitals which each have their own neonatal department for dealing with high-risk deliveries [29]. Prediction of the infant's state at birth determines referrals to level II and III hospitals; however, there are no formal guidelines in Canada for the referral of deliveries to level II or III hospitals.

1.2. Material and Methods

1.2.1. Data

The study was conducted using Quebec provincial data from the Canadian Multi-Regional Cerebral Palsy Registry (CCPR). A detailed description of this unique registry can be found in [14]. Utilizing the framework of the regionalization of pediatric rehabilitation service delivery, children with CP born in 1999 or later were enrolled within six of the province's 17 administrative health regions, capturing approximately half of the province's population within the CCPR. Once cases are identified, parental consent is obtained and maternal medical and obstetric records, as well as the child's neonatal, medical, and rehabilitation records, are reviewed. These data are supplemented by a standardized parental interview and physical examination of the child by a pediatric neurologist, developmental pediatrician, or child physiatrist. For each enrolled child, more than 120 variables are collected and entered into a Research Electronic Database Capture database. In populating the CCPR, local ethics board approval was obtained from each participating institution. The Research Ethics Board at the McGill University Health Center Research Institute provided central approval for CCPR data storage, analysis, and overall operations. To be enrolled in CCPR, a child must be at least two

years of age and meet diagnostic criteria for CP, including a clinical diagnosis of a non-progressive motor impairment resulting from a presumably early insult to the developing brain [12]. A follow-up at 5 years of age is used to confirm the diagnosis and update functional outcome variables.

Children within the CCPR included for analysis in this study were born between 1999 and 2008 in the province of Quebec, which ensured that all participants had a five-year follow-up and confirmation of status available. Children with CP diagnosis linked to any identified post-neonatal cause or cases born outside the province of Quebec were excluded from our investigation.

For our analysis, we classified children according to level of neonatal care available where delivery was carried out [21]. In Quebec maternity care is regionalized and nearly all deliveries take place in public hospitals or birthing centers. Low-risk deliveries are carried out at level I hospitals (well newborn nurseries), level II hospitals (specialty care) or level III hospitals (subspecialty). We used clear, uniform definitions and consistent standards to classify level of neonatal care across the study sites, and appropriate adjustment for differences in case mix between the three groups of hospitals. We classified each delivery unit according to its level of neonatal care using the policy statement on this topic provided by the American Academy of Pediatrics [21] (Appendix 1). This classification reflects differences in the level of obstetric and neonatal competences available at the hospital, outlined in more detail in Appendix 1. In brief, level I centers care for newborns 34 sweeks gestation or more, and can offer intravenous therapy, phototherapy and gavage feeding. Level II centers care for newborns 30 weeks gestation or more, and in addition to level I services can offer ventilation by nasal passage or endotracheal intubation. Level III centers care for newborns regardless of gestational age and in addition to the above services offer nitric oxide therapy, immediate access to pediatric subspecialties, imaging, and surgeries.

The outcome used for this analysis was CP non-ambulatory status, as defined by a Gross Motor Function Classification System (GMFCS) level IV or level V [30]. The major challenge for our research was to control for case-mix differences between types of hospitals. In particular, level II and level III hospitals have a higher proportion of

medium and high-risk pregnancies compared with level I hospitals. We used a quasi-experimental study design [31], controlling for relevant covariates in order to remove selection bias (confounding by indication) that could originate from the differences in case mix between the three groups of hospitals. Our rich dataset allowed us to control for all known biological CP risk factors.

Our data contained a large number of variables about mother and child, allowing us to make appropriate adjustments for differences in case mix between hospitals using propensity score matching. We used current clinical practice guidelines in obstetrics and gynecology [29], perinatal surveillance literature [27] and CP risk factors [32] to choose explanatory variables and make proper adjustments for differences in case mix between hospitals. The following covariates were used to control for risk factors (and deal with selection bias/confounding by indication): birth weight, gestational age, preeclampsia, gestational diabetes, bleeding during pregnancy, severe illness during pregnancy, accident or trauma during pregnancy, preterm birth, a family history of CP, low maternal education (lacking a high school diploma), maternal age, and history of drug use[32], [33]. We also controlled for perinatal asphyxia, which was defined as neonatal encephalopathy with at least three of the following criteria: an Apgar score < 6 at 5 minutes, a cord pH of < 7.0, a cord base excess > 12, an abnormal fetal heart rate such as tachycardia (>160 beats per minute) or bradycardia (<120 beats per minute), presence of meconium, need for intubation, delay in spontaneous respiration, need for resuscitation of the newborn, multisystem involvement in the neonatal period, or abnormal imaging results consistent with hypoxic ischemic injury. We also tested for effect modification relationship between perinatal asphyxia and level of care at delivery. However, the interaction was not statistically significant and post-estimation tests suggested that it did not significantly improve the model's performance. We therefore did not include this interaction term in any subsequent analyses.

Our cohort of 360 children with CP without any post-neonatal cause were born in Quebec between 1999 and 2008. Forty-six percent were born in birth sites with Level III neonatal care, 20% with Level II and the remainder (34%) with Level I neonatal care. Non-ambulatory status (Gross Motor Function Classification System level IV and level V)

was reported in 27% of the cases. The other characteristics of the sample are presented in Table 1.

1.3. Empirical Strategy

1.3.1. Overview

Our empirical objective is to isolate the causal effect of level of neonatal care available at delivery on CP non-ambulatory status. The challenge in examining this research question is that level of neonatal care at delivery is not randomly assigned. We therefore offer an identification strategy that does not rely on random assignment. In particular, we first conduct the analysis assuming that selection on observables holds. Given that we have very rich covariates including all known biological risk factors (which are used by referring doctors), we are rely on selection on observables assumption. However, as a robustness check we also isolate the causal effect of interest under selection on unobservables using instrumental variables.

1.3.2. Model and Assumptions

Let $Y_j = \{Y_j^0, Y_j^1\}$ equal the potential outcome of a child with CP, whose birth was carried out depending on the level of care available at delivery $D_j = \{0,1\}$, where $D = 1$ indicates that birth occurred in a delivery with a superior level of care. For each child we observe only one set of potential outcomes as a function of level of care at delivery:

$$Y_j = Y_j^0 + (Y_j^1 - Y_j^0)D_j.$$

In general, we expect potential outcomes of each child to differ as a function of level of care available at delivery. This implies that the absence of random assignment of level of care at delivery means that we cannot obtain a valid causal estimate of the effect of level of care on non-ambulatory CP status. To see why, consider the non-

experimental comparison between the outcomes of children born in deliveries with different levels of neonatal care. This comparison is:

$$E\left(Y_j \middle| D=1\right) - E\left(Y_j \middle| D=0\right)$$
$$= \left\{E\left(Y_j^1 \middle| D=1\right) - E\left(Y_j^1 \middle| D=0\right)\right\} + \left\{E\left(Y_j^1 \middle| D=0\right) - E\left(Y_j^0 \middle| D=0\right)\right\}$$

where $\left\{E\left(Y_j^1 \middle| D=1\right) - E\left(Y_j^1 \middle| D=0\right)\right\}$

is the average causal effect of level of care available at delivery on outcome Y and the second bracketed term is the bias term, originating from differences in potential outcomes between children who are born in deliveries with different levels of neonatal care. Previous research suggests that this bias term might not be non-zero. Children born within deliveries with higher levels of neonatal care differ greatly in terms of mothers` characteristics, health status and later outcomes. Thus, we can learn little about the causal effect of level of care on children`s CP outcomes by contrasting the outcomes of CP children from birth who received different levels of neonatal care.

To solve this identification problem we invoke the following identifying assumption:

$$Y_j^1, Y_j^0 \perp D_j | X_j,$$

meaning that we assume that potential outcomes in children with CP are conditionally independent of the level of care available at delivery. This assumption states that potential outcomes is as good as randomly assigned to level of care available at delivery given observables. If so, any observed difference in the outcome across level of care available at delivery will reflect the causal effect of neonatal care level on CP non-ambulatory status. Formally we can estimate the causal effect of level of care at delivery on CP non-ambulatory status:

$$E\left(Y_j \middle| X_i, D=1\right) - E\left(Y_j \middle| X_i, D=0\right) = \left\{E\left(Y_j^1 \middle| X_i, D=1\right) - E\left(Y_j^1 \middle| X_i, D=0\right)\right\} +$$
$$\left\{E\left(Y_j^1 \middle| X_i, D=0\right) - E\left(Y_j^0 \middle| X_i, D=0\right)\right\} = \left\{E\left(Y_j^1 \middle| X_i, D=1\right) - E\left(Y_j^1 \middle| X_i, D=0\right)\right\},$$

where the last equality follows from conditional independence assumption.

Is this strategy for identifying the casual effect of type of neonatal care at delivery on CP non-ambulatory status plausible? Our assumption requires that there is no differential effect of neonatal care level at delivery on the latent CP non-ambulatory status. This assumption cannot be directly tested given the fundamental problem of causal inference. However, we can partially assess its validity by testing whether CP non-ambulatory status differs across neonatal level of care at delivery given covariates. We find no evidence that these gaps vary with the level of care at delivery, which lends credibility to the assumption.

1.3.3. Implementation under Exogeneity

Propensity Score Matching (PSM)

We use propensity score matching (PSM) to estimate the effect of level of care at delivery on later CP non-ambulatory status. Along with selection on observables assumption this requires that for all values of the covariates the probability of receiving a treatment (delivery at level II or level III) is strictly positive. Formally this means:

$$P(T = 1|X = x) = e(x),$$

and we assume that $0 < e(x) < 1$.

This permits the estimation of the causal effect of interest via matching strategies as opposed to regression. The first step in conducting the propensity score and subsequent doubly robust estimation is to choose the variables that describe the treatment equation. The treatment equation is defined as the probability of birth within level II or level III care.

Our choice of covariates that would satisfy conditional independence assumption and subsequently specify the treatment equation specification is determined by clinical guidelines published by the Society of Obstetricians and Gynaecologists of Canada,

obstetrical policy documents, the prevailing medical and epidemiological literature as well as informed by clinical judgment[32]–[35]. To our knowledge, there are no guidelines in Canada that outline the decision-making process used to determine whether a birth should be assigned to a specific level of care. We believe that after controlling for covariates listed in Section 2.0, little unobserved heterogeneity is left that is systematically correlated with CP ambulatory status and the treatment assignment.

However, the propensity score estimation also requires that the stable unit treatment value assumption holds. Our data satisfy the stable unit treatment value assumption given that treatment of one birth does not affect the potential CP severity of another individual. We choose a logistic specification for the propensity score model and in particular:

$$P(T = 1|X = x) = \frac{\exp(x\prime\gamma)}{1+\exp(x\prime\gamma)},$$

where X contains covariate set described in Section 2.0. We conduct formal analysis to test the balancing property of the propensity score. Our tests suggest that the balancing property is satisfied and the computation algorithm was restricted to common support under logit model.

The matching process. There are number of approaches to perform propensity score estimations of the casual effect of interest. The use of each method implies a particular tradeoff in terms of bias and efficiency; however, asymptotically all matching algorithms yield the same results. Heckman et al [36] suggest that kernel and local linear matching estimators have the advantage of reduction of the asymptotic mean squared error versus pairwise matching. Kernel matching uses several comparison group members, pairing a treatment case with the weighted average score of all control cases within a certain distance (kernel is the name of the weighting function, and the distance is determined by the bandwidth of the kernel). We implement one-to-one nearest neighborhood, radius matching, kernel matching and local linear regression matching algorithms. We restricted the estimation of average treatment effect on the treated (ATT) on the common support for all matching algorithms. The implementation of different matching algorithms should yield different average treatment effects on the

treated. However, we used bootstrapping, which was repeated 300 times, to derive the bootstrapped standard errors for ATT.

Assessing the common support. We checked common support condition using the density distributions of the propensity scores for births occurred across levels of care. We restricted the analysis to common support condition, and treated individuals who fall outside the common support region were discarded from the analysis.

Evaluation of matching quality. We use several methods to assess whether the distribution of the baseline covariates is similar between different treatment groups such as: standardized bias, Pseudo-R2 and likelihood ratio tests. For each covariate X we compute the standardized bias as suggested by Rosenbaum et al [37].

Assessing the Unconfoundedness Assumption. Our identification framework requires orthogonality between level of neonatal care at delivery and potential CP outcomes given observables. This means that conditional on observed regressors, the selection process into treatment is not related to unmeasured variables that affect the outcome variable, or that confounding by indication can be completely eliminated using the propensity score method. The validity of this assumption cannot be directly tested.

We implement several empirical established approaches in the literature to assess the credibility of this assumption. In particular, we implement Rosenbaum bounds [38] and mhbounds module for Stata [39] to estimate the extent to which the departure from selection on observables may alter reported propensity score estimates. We had also assessed the robustness of the result using several OLS specifications with and without controls.

Ordinary Least Squares (OLS)

We bring this conceptual framework to the data by estimating the following baseline model using OLS:

$$Y_i = \beta_0 + \beta_1 D_j + X_i'\gamma + e_i.$$

Here, Y_i represents CP outcome for child i, D_j is an indicator for level of care at delivery where the child was born. The omitted category is therefore level I care. Vector X_i of controls defined in Section 2.0 The coefficient of interest is β_1 which represents the casual effect of level of care at delivery on CP non-ambulatory status relative to the omitted category of level I care. One concern with the estimation approach is that we may potentially bias estimates of β_1 if unobservable factors have a causal impact on the level of care at delivery; then it may be invalid to treat level of care as good as randomly assigned given the covariates.

Robustness - Alternative Estimation Strategies

We further investigated the robustness of propensity score results using a doubly robust estimation of average treatment effect on the treated. A doubly robust estimation combines outcome regression with weighting by propensity score such that the causal effect of interest is robust to misspecification of one of these models [40], [41]. An estimator is doubly robust if it remains consistent when either a model for the treatment assignment mechanism or a model for the distribution of the counterfactual data is correctly specified.

1.3.4. Results - Analysis under Exogeneity

PSM estimates (average treatment effect on the treated), standard errors and associated 95% confidence intervals are displayed in Table 2. PSM estimates generally pointed to no effect of the level of neonatal care at delivery and later CP non-ambulatory status. There was no statistical significant evidence that delivery carried out in level II or level III hospitals vs level I hospital had any effect on the incidence of CP non-ambulatory status. We found risk estimates for Level II vs Level I, and for Level III vs Level I, to be weakly negative and not statistically significant. A positive and statistically significant risk estimate was found for the Level III vs Level II comparison, suggesting presence of unobserved selection effects. However, the propensity score matching substantially reduced the case-mix differences between the groups of hospitals; absolute standardized bias after adjustments was less than 5% for most risk factors. We reached

similar conclusions via linear probability model, doubly robust estimation and probit model.

A linear probability model did show that several point estimates were statistically significant at conventional levels and are noteworthy (Table 3). These models found a statistically significant association between CP non-ambulatory status and perinatal asphyxia ($p<0.01$), low maternal education ($p<0.1$) and preterm birth ($p<0.1$).

Asphyxia was present in 15% of these children in our cohort; 15.5 % were born at sites with level I neonatal care, 18.6 % of those born at sites with level II neonatal care and 12.6 % born at sites with level III neonatal care. We find that asphyxiated versus non-asphyxiated kids have 2.86 (95% CI 1.57, 5.21) the unadjusted odds of developing a CP non-ambulatory status, while the linear probability model suggests that presence of perinatal asphyxia increases the probability of non-ambulatory status by 27% all else being equal. Preterm birth is found to increase the chances of later CP non-ambulatory status by 9% all else being equal, and low maternal education increased the risk of CP non-ambulatory status by 2%.

1.3.5. Implementation under Endogeneity

Instrumental Variables and Generalized Method of Moments

We implement instrumental variable estimation as robustness check not relying on conditional identifying assumption. Therefore we used multivariate instrumental variables regression along with generalized method of moments, which allows for unobserved risk factors that affect the referral to hospital type and outcomes conditional on that referral, but which often suffers from imprecise estimates. Instrumental variables estimation uses covariates that influence hospital type but which do not influence CP severity. We utilize the mother's residence at birth, using the following indicator variables: indicators for greater Montreal, city of Quebec, Gatineau, Sherbrooke, or indicator for a census metropolitan area. We used Statistics Canada classification of

census metropolitan areas to construct a central metropolitan area indicator as well as Population and Dwellings Counts for Canada.

In other words using instrumental variables we estimate the following first stage equation:

$$D_i = \pi_0 + \pi_1 Z_i + X_i'\pi + \varepsilon_i.$$

The second stage uses as an instrument the predicted probability $\widehat{D_i}$ the main estimating equation is the following (variables where defined above):

$$Y_i = \beta_0 + \beta_1 \widehat{D_i} + X_i'\gamma + e_i$$

Here the first-stage relationship estimates whether the residence at birth influences level of neonatal care at hospital where the delivery was carried out. In order for the IV approach to deliver consistent estimates we need to assume exogeneity and excludability of the instrument. While we had empirically tested both requirements and our results suggest that instruments are very strong and relevant, here we provide the intuition behind our IV approach.

Our expectation is that residence of the mother is a significant factor to influence choice of delivery hospital. In particular, we expect pregnant residing within census metropolitan areas to be more likely to deliver in hospitals with level II, or level III neonatal care as this type of hospitals are located in metropolitan areas. However, we expect type of residence to be orthogonal to unobserved components of CP non-ambulatory status as the type of residence is not systematically related to known determinants of this neurological diseases.

Endogenous Bivariate Probit Model

We also estimate this model using bi-variate probit regression. The first stage can be written:

$$D_i = I[\pi_0 + \pi_1 Z_i + X_i'\pi > \varepsilon_j],$$

where I[.] is the indicator function, and the outcome is determined by:

$$Y_i = I[\beta_0 + \beta_1 D_i + X_i'\gamma > e_i].$$

The correlation between e_i, ε_i is the source of omitted variable bias. The identification requires that excluded instruments Z_i is independent of e_i, ε_i, which are assumed to be normally distributed. Given the distributional assumptions imposed on error terms this model can be estimated using maximum likelihood estimation.

1.3.6. Results - Analysis under Endogeneity

We used instrumental variables methods to produce estimates of the causal effect of secondary care on ambulatory status in children with CP allowing for the non-random assignment into level of care given observable. Our instrumental variables (IV) estimation confirmed no effect relationship between the level of care available at time of delivery and CP non-ambulatory status (Appendices 2-4).

In addition to the causal effect estimate tables includes a number of test statistics assessing the specification of the various models. We report p-values from Hansen J test for overidentifying restrictions, the Anderson-Rubin Wald test of joint significance of the program effects that is robust to weak identification, as well as we report Angrist-Pischke multivariate F-test of excluded instruments. A high F-test and strong rejection failure of the null of valid overidentifying restrictions are signs of strong and valid instruments.

A few patterns emerged in terms of the specification tests. Our instruments are very strong as the F-test is four times above the rule of thumb of 10. We fail to reject the null in the test of overidentification, moreover the instruments are jointly significant. However, the test of endogeneity does not reject the null hypothesis that treatment variable can actually be treated as exogenous regressor. We were satisfied with the overall performance of the instrumental variables models.

We extended the instrumental regression baseline model in two directions in order to assess the sensitivity of the prior findings and to provide additional evidence of the causal effects of treatment on CP ambulatory status. In particular we implemented bivariate endogenous probit model. However, endogenous bivariate probit estimates identified the absence of a relationship between the level of care at birth and CP non-ambulation with the highest precision.

1.4. **Conclusion**

In Quebec, maternity care is regionalized and nearly all deliveries take place in public hospitals. Low-risk deliveries are carried out at level I hospitals including birthing centres, while medium and high-risk deliveries are referred to level II or level III facilities. Prediction of the infant's state at birth determines referrals to level I, II or III hospitals. High-risk deliveries are identified based on unified national medical guidelines [27], [28], [42]. Our study demonstrated that the majority of children developing CP for perinatal reasons were born in birth sites with level III neonatal care. It reflects that, despite the current high level of technology and obstetric and neonatal competencies, outcome of high-risk deliveries referred to birth sites with level III neonatal care, still leads to significant long-term complications. Interestingly, 34% of children developing CP for perinatal reasons were born in sites with Level I neonatal care.

We have shown that differences in the level of neonatal care, and associated medical technology available at the time of delivery, do not seem to be associated with the risk of CP non-ambulatory status. This finding is consistent and robust across methods and empirical specifications used. PSM models showed no statistical significant relationship between the level of neonatal care available at hospital where delivery was carried out and risk of CP non-ambulatory status. This lack of effect was observed for both Level II vs Level I and Level III vs Level I comparisons. Positive coefficients were evident across the Level III vs Level II comparison, which might suggest level II centers are protective; however, this finding reflects the inability of PSM to eliminate unobserved selection effects (unobserved heterogeneity between the two groups of hospitals). Instrumental variables estimation allowed us to control for possible unobserved selection effects and consistently found no relationship between the level of neonatal care at

hospital where delivery was carried out and CP non-ambulatory status. To our knowledge, this is the first study where case mix adjustment was used to study the effects of perinatal regionalization on long-term outcomes using instrumental variables methods.

The lack of incremental impact of the level of neonatal care at the time of delivery on the risk of CP non-ambulatory status likely demonstrates the benefit of the development and generalization of the neonatal resuscitation program (NRP). The NRP educational program for North American healthcare providers working in the delivery rooms and nurseries is designed to aid in learning the cognitive and technical skills required for resuscitation of newborn babies and appropriate referral to specialized centers as soon as possible [43], [44]. Neonatal resuscitation was shown to reduce mortality from intrapartum related events [17], [45], [46], such as perinatal asphyxia, and might explain the lack of effect found in our study. However, the absence of a relationship between CP non-ambulatory status and level of service at delivery might be due to the fact that, within Quebec regionalized maternity service, high-risk deliveries are identified in advance and are subsequently referred to hospitals with an appropriate level of service. This finding is consistent with existing evidence that a regionalized maternity service within a publically-owned and -financed health system does not lead to increased infant morbidity [47], and suggests that medical technology within Quebec's regionalized neonatal-perinatal system is used effectively.

Perinatal asphyxia was highlighted as a significant risk factor for CP non-ambulatory status since asphyxiated versus non-asphyxiated kids have 2.86 the odds of developing a CP non-ambulatory status. In our cohort, the percentage of children with perinatal asphyxia born in each of the three neonatal care levels were approximately equal, being 15.5%, 18.6% and 12.6% in levels I, II and III respectively. However, non-ambulatory status was more unevenly distributed, present in 28.5% of kids born in level I, 20.0% of kids born in level II, and 29.3% of kids born in deliveries with level III care. Perinatal asphyxia cannot be predicted before birth, and thus has to be acutely managed in hospitals with different levels of technology and obstetric and neonatal competencies available for neonatal care. The type of therapy the child receives immediately after birth is an important determinant of later CP severity. Newborns with perinatal asphyxia born

in level I hospitals are usually transferred to level II or III hospitals, with the capacity to provide an increased level of further care such therapeutic hypothermia. It is important to note that therapeutic hypothermia became widely available in Quebec as of 2009, so the birth cohort included in this study did not have this therapeutic option available at the time of their delivery. Failure to recognize the patients that could potentially benefit from this treatment remains a challenge, since there is a narrow window of opportunity to act. As the proportion of births complicated by perinatal asphyxia among children with CP was evenly distributed among levels of neonatal care available at birth sites, it would be of interest to study the impact of lack of local availability of therapeutic hypothermia in level I centers on later risk of non-ambulatory status. Our results also indicate that preterm birth and low maternal education may constitute important independent risk factors for CP non-ambulatory status which deserve further investigation. We believe that our study has strong external validity and that these results might apply to many countries with regionalized systems of perinatal care such as the U.S., Norway and other European countries.

Our study has several limitations. The methods employed cannot replace a randomized controlled trial (RCT), and may not have fully controlled for selection effects or unobserved covariates. However, an RCT that would assess the impact of levels of neonatal care available at hospitals where delivery was carried out on CP ambulatory status is likely not to be undertaken given ethical and pragmatic concerns. Our study does not discusses differences in other measures that might be important as well for determination of outcomes of regionalized perinatal care such as fine motor skills, cognition, language, or behaviour.

In conclusion, our study implies that the level of technology available at delivery does not incrementally affect the distribution of CP non-ambulatory cases. The success of the neonatal resuscitation program and referral of high risk births to regional hospitals with sufficient obstetric and perinatal competence and resources may contribute to this lack of relationship. This suggests that level of care and associated medical technology within the Quebec regionalized neonatal-perinatal system, is used effectively, since it does not offer any further marginal benefit in the reduction of severe CP outcomes. The system works well as it is and this is supportive of the perinatal regionalization. Further

research is needed to understand the causal links and associated mechanisms between prenatal risk factors, perinatal asphyxia and CP severity.

Table 1-1. General Characteristics of the Population

VARIABLES	n = 360 children with CP
Level of Service at Delivery	
Level I, n (%)	123 (34.17)
Level II, n (%)	70 (19.44)
Level III, n (%)	167 (46.39)
Non-Ambulatory Status (GMFCS IV-V), n(%)	98 (27.22)
Maternal Age, mean ± SD	29.64 ± 5.05
Mother's ethnic group	
Caucasian	292(81.11)
Other	68 (18.89)
Education	
High school or more education	319 (88.6)
Less than high school education	41 (11.4)
Family History of CP, n (%)	17 (4.72)
History of Stillbirths, n (%)	27 (7.50)
Type of Pregnancy	
Single foetus	319 (88.61)
Pre-eclampsia, n (%)	27 (7.50)
Gestational Diabetes, n (%)	52 (14.44)
Bleeding during Pregnancy, n (%)	98 (27.22)
Severe Illness during Pregnancy, n (%)	78 (21.67)
Accident or Trauma during Pregnancy, n (%)	58 (16.11)
Birth weight (gram), mean ± SD	2594.78 ±1039.17
Gestational age (weeks), mean ± SD	35.5 ± 0.27
Prematurity (<37 weeks), n (%)	151(41.94)
Perinatal Asphyxia, n (%)	53 (14.72)

Table 1-2. Propensity Score Matching Results

LEVELS	Radius: caliper=0.1	Kernel	LLR EpanK	LLR NormalK
II vs I	-0.104	-0.081	-0.085	-0.082
	[0.071]	[0.070]	[0.217]	[0.071]
III vs I	-0.054	-0.072	-0.024	-0.086
	[0.069]	[0.078]	[1.238]	[0.076]
III, II vs I	-0.037	-0.06	-0.04	-0.06
	[0.06]	[0.06]	[0.05]	[0.06]

Note. *** p<0.01, ** p<0.05, * p<0.1. Bootstrapped Standard Errors in brackets (300 repetitions). LLR – local linear regression. EpanK - The Epanechnikov Kernel. NormalK - The Gaussian Kernel. In all models less than 10% observations were excluded due to imposition of the common support condition.

Table 1-3. Linear Probability Model Results

VARIABLES	Linear regression
Level II	-0.072
	[0.063]
Level III	-0.012
	[0.057]
Pre-eclampsia	0.030
	[0.073]
Gestational diabetes	-0.031
	[0.067]
Bleeding during pregnancy	-0.033
	[0.054]
Severe illness during pregnancy	-0.037
	[0.054]
Accident/ trauma during pregnancy	0.017
	[0.057]
Preterm birth	0.092*
	[0.05]
Birth weight	.0001
	[.001]
Family history of CP	0.041
	[0.089]
Maternal education	-0.024*
	[0.013]
Maternal age	0.003
	[0.005]
Drugs	0.061
	[0.113]
Observations	358

Note. *** p<0.01, ** p<0.05, * p<0.1. Level I hospitals are the base category. Robust standard errors in brackets. Join F-test of level II and level III being excludable p-value=0.394. Statistical Power=0.76.

Table 1-4. Instrumental Variables Results (Level II vs Level I)

LEVELS	2-Step GMM	Endogenous bivariate probit
II vs I	-0.0073	0.006
	[0.134]	[0.031]
Observations	192	192
Overid	0.215	
Overid P-val	0.889	
F-test	58.91	
AR	0.061	
AR P-val	0.979	
Endog	0.258	
Endog P-val	0.612	
Rho		-0.704
		[0.611]
Chi-sq		0.001
F-analog		12.31
Exon P-val		0.914

Note. *** p<0.01, ** p<0.05, * p<0.1. Table presents reduced form estimates of the effects of interest from two stage least squares, generalized method of moments, endogenous bivariate probit. Robust standard errors in brackets. Over is the Hansen J test for overidentification; AR is the Anderson-Rubin (1949) Wald test of the joint significance of the endogenous regressors; Endog is a test for endogeneity of exposure variable; F-test is Angrist-Pischke multivariate F-test of excluded instruments; Chi-sq is Wald test of Rho=0. F-analog is the test of joint significance of instrumental variables. Exon P-val is the smallest *p-value* of the excluded instrument in the regression of residuals on covariates and instrumental variables. 2SLS estimates are numerically equivalent 2-Step GMM up to two decimal places.

Table 1-5. First Stage (Level II vs Level I)

VARIABLES	Linear regression
Census Metropolitan Area Indicator	0.696***
	[0.079]
Montreal Indicator	0.576***
	[0.091]
City of Quebec Indicator	0.956***
	[0.069]
Pre-eclampsia	-0.097
	[0.093]
Gestational diabetes	-0.056
	[0.097]
Bleeding during pregnancy	-0.326
	[0.161]
Severe illness during pregnancy	0.019
	[0.082]
Accident/ trauma during pregnancy	0.102
	[0.086]
Preterm birth	0.033
	[0.121]
Birth weight	-0.205
	[0.186]
Family history of CP	-0.026
	[0.128]
Maternal education	0.006
	[0.041]
Maternal age	-0.012
	[0.006]
Drugs	-0.213
	[0.188]
Observations	192

Note. *** p<0.01, ** p<0.05, * p<0.1. Robust standard errors in brackets. Centered R-squared=0.31.

Table 1-6. Instrumental Variables Results (Level III vs Level I)

LEVELS	2-Step GMM	Endogenous bivariate probit
III vs I	0.04	0.0039
	[0.127]	[0.026]
Observations	287	287
Overid	0.541	
Overid P-val	0.763	
F-test	39	
AR	0.22	
AR P-val	0.889	
Endog	0.264	
Endog P-val	0.607	
Rho		-0.188
		[0.2327]
Chi-sq		0.639
F-analog		480
Exon P-val		0.240

Note. Table presents reduced form estimates of the effects of interest from two stage least squares, generalized method of moments, endogenous bivariate probit. Robust standard errors in brackets. *** p < 0.01, ** p < 0.05. Over is the Hansen J test for overidentification; AR is the Anderson-Rubin (1949) Wald test of the joint significance of the endogenous regressors; Endog is a test for endogeneity of exposure variable; F-test is Angrist-Pischke multivariate F-test of excluded instruments; Chi-sq is Wald test of Rho=0. F-analog is the test of joint significance of instrumental variables. Exon P-val is the smallest p-value of the excluded instrument in the regression of residuals on covariates and instrumental variables. 2SLS estimates are numerically equivalent 2-Step GMM up to two decimal places.

Table 1-7. First Stage (Level III vs Level I)

VARIABLES	Linear regression
Census Metropolitan Area Indicator	0.611***
	[0.069]
Montreal Indicator	0.287 ***
	[0.064]
City of Quebec Indicator	0.165***
	0.007
Pre-eclampsia	-0.032
	[0.071]
Gestational diabetes	-0.027
	[0.088]
Bleeding during pregnancy	-0.083
	[0.070]
Severe illness during pregnancy	-0.025
	[0.061]
Accident/ trauma during pregnancy	-0.040
	[0.058]
Preterm birth	-0.072
	[0.1035]
Birth weight	-0.148
	[0.119]
Family history of CP	0.058
	[0.070]
Maternal education	-0.012
	[0.027]
Maternal age	0.131
	[0.110]
Drugs	-0.065
	[0.102]
Observations	287

Note. *** p<0.01, ** p<0.05, * p<0.1. Robust standard errors in brackets. Centered R-squared=0.34.

Table 1-8. Instrumental Variables Results (Levels III and II vs Level I)

LEVELS	2-Step GMM	Endogenous bivariate probit
III vs II	0.012	0.001
	[0.105]	[0.020]
Observations	235	235
Overid	0.280	
Overid P-val	0.97	
F-test	63.80	
AR	0.59	
AR P-val	0.67	
Endog	0.821	
Endog P-val	0.365	
Rho		0.20
		[0.57]
Chi-sq		0.7342
F-analog		61.06
Exon P-val		0.389

Note. Table presents reduced form estimates of the effects of interest from two stage least squares, generalized method of moments, endogenous bivariate probit. Robust standard errors in brackets. *** $p < 0.01$, ** $p < 0.05$. Over is the Hansen J test for overidentification; AR is the Anderson-Rubin (1949) Wald test of the joint significance of the endogenous regressors; Endog is a test for endogeneity of exposure variable; F-test is Angrist-Pischke multivariate F-test of excluded instruments; Chi-sq is Wald test of Rho=0. F-analog is the test of joint significance of instrumental variables. Exon P-val is the smallest *p-value* of the excluded instrument in the regression of residuals on covariates and instrumental variables. 2SLS estimates are numerically equivalent 2-Step GMM up to two decimal places.

Table 1-9. First Stage (Level III vs Level II)

VARIABLES	Linear regression
Montreal Indicator	0.649***
	[0.054]
City of Quebec Indicator	0.942**
	[0.108]
Sherbrook Indicator	0.951***
	[0.050]
Perinatal asphyxia	0.045
	[0.085]
Pre-eclampsia	0.050
	[0.069]
Gestational diabetes	-0.027
	[0.088]
Bleeding during pregnancy	0.025
	[0.085]
Severe illness during pregnancy	-0.054
	[0.060]
Accident/ trauma during pregnancy	-0.067
	[0.062]
Preterm birth	-0.109
	[0.107]
Birth weight	0.036
	[0.111]
Family history of CP	0.169*
	[0.089]
Maternal education	0.175
	[0.098]
Maternal age	0.009*
	[0.004]
Drugs	0.046
	[0.165]
Observations	235

Note. *** p<0.01, ** p<0.05, * p<0.1. Robust standard errors in brackets. . Centered R-squared=0.44.

Chapter 2.

Interhospital Transfers and Long Term Health Outcomes within a Regionalized Neonatal-Perinatal System. Evidence from a Population based Cerebral Palsy Registry.

2.1. Introduction

The transport of critically ill neonates has always been seen to be an integral part of a regionalized perinatal-neonatal system. An optimal neonatal transport system should be able to rapidly deliver critical care to the patient's bedside at the referring hospital and of maintaining that level of care during transport to the receiving hospital[48]. However, in Canada it has long been recognized that not all such movements have occurred under optimal circumstances`[49].

In our previous paper we found that controlling for observed and unobserved risk factors, differences in the levels of care at birth sites, and associated complexity of available neonatal-perinatal technology, are not associated with differences in Cerebral Palsy (CP) severity. The success of the neonatal resuscitation program and referral of high-risk births to regional hospitals with sufficient obstetric and perinatal competence may help to explain this finding. Thus, our aim in this study was to further investigate this result by looking at the effect of interthospital transfers in the context of Quebec regionalized neonatal-perinatal system. Specifically, we aimed to answer the following question: do interhospital transfers reduce the incidence of the most sever CP cases?

This study evaluates the impact of interhospital neonatal transfers on the long-term neurodevelopmental outcomes of children with CP. The level of care at delivery hospital determines the type of therapy newborns receive immediately after birth. The

type of therapy is critical to prevent or treat adverse events around labor and delivery which determine later neurological and neurocognitive impairments such as CP and its severity. Critically ill newborn patients are transported to alternate hospitals to obtain additional care, whether technical, professional or procedural care, that is not available at the existing location. Specifically, we sought to evaluate the relationship between neonatal transfers and later CP non-ambulatory status, using data from the Canadian Multi-Regional Cerebral Palsy Registry (CCPR).

2.2. Material and Methods

2.2.1. Data

The study was conducted using Quebec provincial data from the CCPR. A detailed description of this unique registry can be found in [14]. Children within the CCPR included for analysis in this study were born between 1999 and 2008 in the province of Quebec, which ensured that all participants had a five-year follow-up and confirmation of status available. Children with CP diagnosis linked to any identified post-neonatal cause or cases born outside the province of Quebec were excluded from our investigation.

For our analysis, we were interested in postnatal interhospital transfers, we thus ignored the intrahospital movements. We classified children according to whether the kid had been transferred to a different hospital after birth (level I to level II, or level I to level III). In Quebec maternity care is regionalized and nearly all deliveries take place in public hospitals or birthing centers. Low-risk deliveries are carried out at level I hospitals (well newborn nurseries), level II hospitals (specialty care) or level III hospitals (subspecialty). We used clear, uniform definitions and consistent standards to classify level of neonatal care across the study sites, and appropriate adjustment for differences in case mix between the three groups of hospitals. We classified each delivery unit according to its level of neonatal care using the policy statement on this topic provided by the American Academy of Pediatrics [21]. This classification reflects differences in the level of obstetric and neonatal competences available at the birth hospital.

This classification reflects differences in the level of obstetric and neonatal competences available at the hospital. In brief, level I centers care for newborns 34 weeks gestation or more, and can offer intravenous therapy, phototherapy and gavage feeding. Level II centers care for newborns 30 weeks gestation or more, and in addition to level I services can offer ventilation by nasal passage or endotracheal intubation. Level III centers care for newborns regardless of gestational age and in addition to the above services offer nitric oxide therapy, immediate access to pediatric subspecialties, imaging, and surgeries.

Interfacility transport of neonatal patients for advanced or specialty medical care is an integral part of North America health care delivery system[50]. Critically ill newborns are transported to alternate locations to obtain additional care, whether technical, cognitive, or procedural, that is not available at the existing location[50]–[52].

However, the decision to transport critically ill newborns to another facility, is based on a comprehensive assessment of the potential risks inherent during transport and follows specific American Academy of Pediatrics recommendations for pediatric transport systems[48] and Canadian Association of Paediatric Health Centres recommendations for a minimum set of standards[50]. Critically ill newborns are at increased risk of morbidity and mortality during transport[52]–[54]. Risk can be minimized and outcomes improved with careful planning, the use of appropriately qualified personnel, and availability of equipment [51], [55]. The expected benefits of transport must be weighed against the possible risks during the transport. However, financial considerations are not a factor when contemplating moving a critically ill newborn in Canada.

The outcome used for this analysis was CP non-ambulatory status, as defined by a Gross Motor Function Classification System (GMFCS) level IV or level V [30]. The major challenge for our research was to control for case-mix differences between types of hospitals. In particular, level II and level III hospitals have a higher proportion of medium and high-risk pregnancies compared with level I hospitals. We used a quasi-experimental study design [31], controlling for relevant covariates in order to remove selection bias (confounding by indication) that could originate from the differences in

case mix between the three groups of hospitals. Our rich dataset allowed us to control for all known biological CP risk factors.

Our data contained a large number of variables about mother and child, allowing us to make appropriate adjustments for different clinical needs using methods based on selection on observables. We used current clinical practice guidelines in obstetrics and gynecology [29], perinatal surveillance literature [27] , CP risk factors [32], the American Academy of Pediatrics recommendations for pediatric transport systems[48] and Canadian Association of Paediatric Health Centres recommendations for a minimum set of standards[50] to choose explanatory variables to describe the decision to transport a critically ill newborns to another facility. The following covariates were used to control for risk factors (and deal with selection bias/confounding by indication): neonatal encephalopathy, assisted delivery, multiple fetuses, preterm birth, intrauterine infection, toxic exposure, maternal illness.

Our cohort of 322 children with CP without any post-neonatal cause were born in Quebec between 1999 and 2008. Forty-six percent were born in birth sites with Level III neonatal care, 20% with Level II and the remainder (34%) with Level I neonatal care. Non-ambulatory status (Gross Motor Function Classification System level IV and level V) was reported in 27% of the cases. 18% out of 322 children with CP had an interhospital transfer, meaning that these were born in level I hospital and transferred after birth to a level II or level III facility.

2.3. **Empirical Strategy Overview**

Our empirical objective is to isolate the causal effect of interhospital transfers on later CP non-ambulatory status. The challenge in examining this research question is that neonatal transfers are not randomly assigned. Neonatal transfers' decision follow clinical consensus guidelines. We therefore offer an identification strategy that does not rely on random assignment. In particular, we conduct the analysis assuming that selection on observables holds. Given that we have very rich covariates including all known biological risk factors used by referring clinicians, selection on observables assumption can be invoked.

2.3.1. Model and Assumptions

Let $Y_j = \{Y_j^0, Y_j^1\}$ equal the potential outcome of a child with CP, who might have been transferred $D_j = \{0,1\}$, where $D = 1$ indicates that child had been transferred. For each child we observe only one set of potential outcomes as a function of transfer decision: $Y_j = Y_j^0 + (Y_j^1 - Y_j^0)D_j$.

In general, we expect potential outcomes of each child to differ as a function of interhospital transfer. This implies that the absence of random assignment of neonatal transfer means that we cannot obtain a valid causal estimate of the effect of transfer on non-ambulatory CP status. To see why, consider the non-experimental comparison between the outcomes of transferred and non-transferred children. This comparison is:

$$E(Y_j|D = 1) - E(Y_j|D = 0)$$
$$= \{E(Y_j^1|D = 1) - E(Y_j^1|D = 0)\} + \{E(Y_j^1|D = 0) - E(Y_j^0|D = 0)\}$$

where $\{E(Y_j^1|D = 1) - E(Y_j^1|D = 0)\}$ is the average causal effect of level of care available at delivery on outcome Y and the second bracketed term is the bias term. Previous clinical research suggests that this bias term might not be non-zero. Children transferred after birth might differ greatly in terms of neonatal health status and later CP outcomes. Thus, we can learn little about the causal effect of transfer on children`s CP outcomes by contrasting the outcomes of CP children from whose who had been and had not been transferred.

To solve this identification problem we invoke the following identifying assumption:

$$Y_j^1, Y_j^0 \perp D_j|X_j,$$

meaning that we assume that potential outcomes in children with CP are conditionally independent of the neonatal transfer. This assumption states that potential outcomes is as good as randomly assigned to transfers given observables. If so, any

observed difference in the outcome will reflect the causal effect of neonatal transfer on CP non-ambulatory status. Formally we can estimate the causal effect of transfer at delivery on CP non-ambulatory status:

$$E\left(Y_j \middle| X_i, D=1\right) - E\left(Y_j \middle| X_i, D=0\right) = \left\{E\left(Y_j^1 \middle| X_i, D=1\right) - E\left(Y_j^1 \middle| X_i, D=0\right)\right\} + \left\{E\left(Y_j^1 \middle| X_i, D=0\right) - E\left(Y_j^0 \middle| X_i, D=0\right)\right\} = \left\{E\left(Y_j^1 \middle| X_i, D=1\right) - E\left(Y_j^1 \middle| X_i, D=0\right)\right\},$$

where the last equality follows from conditional independence assumption.

Is this strategy for identifying the casual effect of neonatal transfer on CP non-ambulatory status plausible? Our assumption requires that there is no differential effect of neonatal transfer on the latent CP non-ambulatory status. This assumption cannot be directly tested given the fundamental problem of causal inference[56].

2.3.2. Implementation under Exogeneity

Propensity Score Matching (PSM)

We use propensity score matching (PSM) to estimate the effect of transfers on later CP non-ambulatory status. Along with selection on observables assumption this requires that for all values of the covariates the probability of receiving a neonatal transfer is strictly positive.

Ordinary Least Squares (OLS) and Propensity score matching

We estimate the following baseline model using OLS:

$$Y_i = \beta_0 + \beta_1 D_j + \beta_2 P(X) + e_i.$$

Here, Y_i represents CP outcome for child i, D_j is an indicator for neonatal transfer. Vector X_i of controls and $P(X)$ is the propensity score. The coefficient of interest is β_1 which represents the casual effect of neonatal transfer.

However, we also estimate an alternative model:

$$Y_i = \beta_0 + \beta_1 D_j + \beta_2 P(X) + \beta_3 I_j + e_i.$$

Here, I_j represents the interaction term transfers on the overlap region. This estimation circumvents the comparison between transferred and non-transferred on the region where propensity scores for the two groups overlap.

2.4. **Results**

18% out of 322 children with CP had an interhospital transfer, meaning that these were born in level I hospital and transferred after birth to a level II or level III facility. PSM estimates (average treatment effect on the treated), standard errors and associated 95% confidence intervals are displayed in Table 2. PSM estimates generally pointed to no statistical effect of neonatal transfers and later CP non-ambulatory status. However, the propensity score matching estimates are negative and the standards errors are large.

The two linear probability models show that neonatal transfers' estimates while negative were not statistically significant at conventional levels (Table 3). However, model 2 identifies no effect with a slighter smaller standard errors suggestive that effect identification might not possible because of a small sample size.

We further investigated the relationship by computing time travel by car between inborn and out born facilities. We found that total travel time for all children who were transferred immediately after birth were less than the critical period of five hours, and for 95% of all transfers the total travel time was less than one and a half hours. This implies that the effect of transfers in principle cannot be detected by default given that all neonates who needed a transfer did got transferred.

2.5. Conclusion

Interthospital transfers are an integral part of the Quebec regionalized neonatal-perinatal system. The decision to transport a critically ill newborn or to another facility, is based on an assessment of the potential benefits of transport weighed against the potential risks and follows clinical practice guidelines and recommendations for a minimum set of standards[48], [50], [54], [51].

The interhospital transfer point estimates were negative and not statistically significant. Further investigation had shown that the effect of transfers cannot be detected given that all neonates who needed a transfer did get one. The identification of the interhospital transfers would require a richer dataset which would contain data on the outcomes of kids who required a transfer but never got one.

Table 2-1 Linear Probability Model Results

VARIABLES	Linear regression
Transfer	-0.08
	[0.12]
P(X)	0.47
	[0.68]
Observations	322

Note. *** p<0.01, ** p<0.05, * p<0.1. Level I hospitals are the base category. Robust standard errors in brackets. Join F-test of level II and level III being excludable p-value=0.39.

Table 2-2 Linear Probability Model Results

VARIABLES	Linear regression
Interaction	-0.087
	[0.11]
P(X)	0.29
	[0.70]
Observations	322

Note. *** p<0.01, ** p<0.05, * p<0.1. Level I hospitals are the base category. Robust standard errors in brackets. Join F-test of level II and level III being excludable p-value=0.38. Statistical Power=0.70.

Chapter 3.

Nutrition assistance programs Early Skills Formation: Evidence from a Community Based Large Pregnant Cohort

3.1. Introduction

Human capital is an essential source of long term economic growth [57], [58]. Building upon seminal contributions by Schultz and Becker [59], [60], Cunha and Heckman [61] have argued that human capital production and skill formation is a life cycle process which begins in the womb and continues throughout life. An increasingly interdisciplinary body of evidence shows that gaps in skills originating from birth through the age of five determine the lifetime skill formation process, and long term economic, health and social outcomes [62]–[65]. The economics, psychological and clinical literature offers some guidance toward the causal relationships underlying early skills formation; however, the mechanisms of cognitive and non-cognitive skill formation outcomes remains to be been established. A central question of interest is whether skill formation technology depends on improved nutrition in early childhood. If so, it is conceivable that policymakers can reduce ability gaps between children from various socioeconomic groups and ultimately raise the productivity of society at large through nutrition interventions at an early age.

A large body of research shows that skill formation is a highly complex process influenced by environmental, genetic, and epigenetic factors in perinatal and postnatal periods [66], [67]. Understanding the role and related mechanisms of nutritional interventions on early skills formation is critical. The existing scientific literature, using evidence from animal models, demonstrates that early nutrient deficiencies have substantial, long-lasting negative effects on early brain development [68]–[70]. Some

nutrients appear to be more important than others for brain development; however, evidence that there are *critical* and *sensitive* periods in brain synaptic plasticity is overwhelming[63].

The study of skill formation through the nutritional channel is even more important in human beings due to dynamic complementarity of the skills formation process [61]. Thus, if a child does not receive appropriate nutrients during early childhood, it may be very difficult or even impossible to appropriately support brain plasticity [71] which ultimately results in poor neurocognitive outcomes at a later age. Better nutrition during childhood is also associated with better health and educational outcomes in children [72]–[75]. However, there is compelling evidence that the first two years of a child's life is thought to be the critical period when nutrition has the greatest effect on child health, growth and development [71], [76]. The study reported here is to our knowledge the first to use detailed data on prenatal, perinatal and postneonatal nutritional exposures and developmental outcomes during these critical years.

The literature establishes that in the United States food and nutrition assistance programs are linked to improved neonatal outcomes [77]–[80] and long term outcomes [81]. However, virtually no evidence exists regarding whether federal or local food programs in the U.S. are associated with early developmental outcomes. We are aware of only one study that has assessed the direct of WIC on IQ and cognitive test scores in early childhood [82]. These authors reported positive effects of prenatal WIC on cognitive development. We address this gap by analyzing data from a large prospective, community-based study of mother-infant pairs to estimate the effect of participation in federal funded nutrition assistance programs on early cognitive and non-cognitive developmental outcomes.

In this paper, we estimate the effect of mothers' participation in the Supplementary Nutrition Assistance Program (SNAP) and the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) on early cognitive and non-cognitive developmental outcomes as measured by the Bayley Scales of Infant Development (BSID-III). Our data are from a large, prospective, community-based panel study of mother-infant pairs. In this rich data set we can directly identify the change in

neurodevelopmental outcomes associated with changes in food programs uptake. In a model where unobserved heterogeneity only affects the level of neurodevelopmental outcomes this can be interpreted as a causal effect.

The challenge of identifying the causal effect in question is that mothers' participation in nutrition assistance programs is not assigned randomly. The main limitation of most food programs research is the inability to remove the selection bias resulting from mothers choosing whether or not to participate in federal food assistance programs. In particular the literature has struggled to find credible and strong instrumental variables for participation in food programs [79]. This paper addresses these methodological limitations and aims to remove selection bias by employing fixed effects models. Our unique dataset allows us to control for known early development risk factors in the analysis and previously unavailable biological risk factors, anthropometric measures and parental environments.

We take advantage of the panel structure of the data and a rich set of time-varying control variables on child, caregiver, home and other contextual variables to estimate the effect of interest using fixed effects models. In particular, to deal with the selection problem we use mother-infant fixed-effects (FE) models, which compare child outcomes over time among mothers who participate in federal food assistance programs and those who do not participate. This technique uses variation in program participation status over time and it controls for unobserved mother-infant pair characteristics, and for family and environmental background attributes that are time-invariant. In addition, we control for a wide range of time-varying mother, family background and child characteristics. The causal relationship between federal assistance programs' uptake and child outcomes is identified under the assumption that the differences in uptake are exogenous to cognitive and non-cognitive outcomes after controlling for these time-varying characteristics. We build on previous research which has found a positive relationship between participation in federal nutrition assistance programs and health outcomes [77]–[81], [83].

We find that mothers' participation in SNAP and WIC during pregnancy and in early childhood has a direct effect on cognitive and noncognitive skill formation in early

age. We find that participation in food assistance programs leads to a significant increase in receptive communication as measured by Bayley scales. Our results are robust, and the inclusion of a rich set of possible confounding factors further supports the validity of the research design.

This paper makes important contributions to both the economics literature on skill formation and to the body of research which links the expansion of resources in utero and during childhood to health and socio-economic outcomes. First, the literature to date has not considered the effect of participation in food assistance programs during pregnancy and early childhood on cognitive and noncognitive skill formation in the early years. Rather, it has focused on the impact of food assistance programs on neonatal and long-term outcomes. We show that uptake of food assistance programs is associated with improved Bayley scores for children. Second, we explore the biological mechanisms which may underlie our findings, a completely novel approach to the literature as far as we are aware. We show that mothers' participation in food assistance programs increases intake of those nutrients associated with early childhood development such as iron, zinc and omega-3.

We use the Bayley Scales of Infant Development (BSID-III), a set of standardized measures commonly used within the field of developmental science for analyzing short- to medium-term outcomes of babies. The BSID's main use is to detect delays in neurodevelopment [84]. The BSID-III is a widely-accepted developmental assessment instrument for children ages birth to 42 months [85]. The BSID is a global measure of developmental status in infancy that assesses and aggregates the timely attainment of relatively crude milestones in infancy and early childhood.

The remainder of our paper is as follows. In Section 2 we summarize the economic literature on the long term effects of early skill formation interventions. In Section 3 we summarize the biological science literature in order to provide guidance for econometric model building. In Section 4 we provide background information on the US federal and community food assistance programs. In Section 5 we describe our data. In Section 6 we present our econometrics framework and motivate the empirical strategy and in Section 7 our results. We conclude in Section 8.

3.2. Early skill formation

Evidence on the importance of ability in determining long term socio-economic success is overwhelming. Interdisciplinary research have shown the existence of critical and sensitive periods in the formation of skills [86], [87]. Persistent and substantial gaps in non-cognitive and cognitive abilities determine a variety of outcomes and have a direct effect on wages, schooling, teen pregnancies and other socio-economic outcomes [88]. However, early skill formation is critical as numerous studies in economics, human development have documented that cognitive and non-cognitive skills are produced in the early years of childhood [61], [65], [89]–[92].

Existing research documents that the technology of skill formation is self-productive and complementary. Self-productivity means that the formation of skills has a higher return if the higher the stock of skills at the previous period is available, while complementary implies that early investment facilitates the productivity of later investment, as skills beget skills in a complementary and dynamic way [61]. However, complementarity, self-productivity means no equity-efficiency trade-off for early investments [61]. This implies that returns to late childhood investment and remediation in later years are low. If a child does not receive the appropriate stimulation during early childhood period, it may be very difficult to develop certain functions at a later age associated with improved socio-economics outcomes.

3.3. Nutrition and Early Skill Formation

Fetal, neonatal and postnatal period is a time of rapid brain development (neuroplasticity), and of critical acquisition of cognitive development, and interpersonal skills [93], [94]. Evidence that nutrition is a direct biological and a mediation factor in brain growth and development is abundant in scientific literature. A range of *in vitro* and *in vivo* animal models have been used to characterize the mechanistic linkages between nutritional deficiencies to structural and/or functional alterations in neurodevelopment and impact on behavior [68]. More recently, the epigenetic effects of nutrients had been documented in emergent genetic literature [95], [96].

Extensive epidemiological, economics, health sciences literature has explored the role of nutrition, early childhood, and its relationship to health outcomes in adulthood. Given the fundamental role of nutrients in supporting all aspects of structural and functional brain development, food assistance programs provide essential nutrients that must be introduced by diet since they cannot be synthesized by the organism. Lack of nutrition would have a negative influence on all aspects of development and can lead to adaptive physiologic responses that impair development with long-term consequences [97], [98].

Supplemental Assistance for Needy Families (SNAP) and The Special Supplemental Nutrition Program for Woman, Infants, and Children (WIC) are the two fundamental safety net federally funded programs with combined spending of $82.85 billions per year[99]. SNAP is the only public assistance program that is available to all income eligible families was rolled out between 1962 and 1975, providing low-income families vouchers that could be used at grocery stores to purchase food. WIC program aims to increase nutritional well-being among low-income pregnant/post-partum women, infants and young children. Established in 1972, the program offers three types free of charge benefits to participants: a supplemental food package, nutrition education, and referrals to health care and other services [100]. These packages included combinations of the following foods: iron-fortified infant formula; iron-fortified infant and adult cereal; vitamin C-rich fruit juice and/or vegetable juice; eggs; milk; cheese; peanut butter and/or dried beans or peas; tuna; and carrots. Special infant formulas and certain medical foods could also be provided by the WIC food package when prescribed by a physician or health professional for a specific medical condition. Existing research links participation in SNAP or WIC to health outcomes. The literature has focused on critical birth outcomes, such as low birthweight, preterm delivery, and infant mortality [77], [79], [81], [101].

Much of the research on SNAP's and WIC's effect on participants' health face a number of methodological challenges, in addition to issues of selection bias. Many outcomes develop over a long period and may require to control for the complex interplay of diet, and environment. Furthermore, economic theory suggests that relationship between federal, or local programs, associated eligibility criteria would

induce individuals to optimize decisions related to participation in different programs. For example, a majority of WIC participants also use other assistance programs, such as Medicaid, SNAP. Moreover, the impact of local food programs on health or developmental outcomes is largely unknown. This requires to ascertain whether observed effect is due to WIC or SNAP or to other programs.

3.4. Material and Methods

3.4.1. Data

The study was conducted using data from Conditions Affecting Neurocognitive Development and Learning in Early Childhood study (CANDLE). CANDLE is a prospective longitudinal study of early cognitive development which extends from the second trimester of pregnancy until the child reaches age 4 [102]. CANDLE recruited 1,503 healthy pregnant women between 16.0 and 28.0 weeks of gestation, who had normal singleton fetal pregnancies and lived in Shelby County, TN [102]. The selection criteria for our study included the inclusion criteria for the CANDLE study.

While the primary focus of the CANDLE study is child cognitive development, it has collected detailed information on parental environments; maternal psychosocial status; caregiver functioning; caregiver-child interaction; maternal, newborn, and postnatal anthropometric measures; and clinical information. Maternal and family data were collected at the second and third trimesters of pregnancy. During a home visit at 4 weeks postpartum (home visit 1 or HV1), CANDLE study personnel collect child health updates. The mother and the child make annual visits to the study clinics for cognitive, psychosocial, and clinical assessments. Additional health information from participants and other updates are collected using telephone interviews, which are regularly scheduled between annual visits. Demographic and phenotypic data on the mothers and newborns were also abstracted from clinical records. This research was approved by the Institutional Review Board of the University of Tennessee Health Science Center, and informed consent was obtained from all mothers.

Table 1 provides an overview of our data. In the full sample, 62% of the mothers were of African American race, 48% of mothers were on Medicaid of TennCare insurance, 47% with annual reported income is less than $24999, 47% married, 9% reported tobacco use and 49 had a high school diploma. 50% of mothers report participation in WIC and 44% participation in SNAP, however, uptake in WIC declines over time much more than in SNAP. In particular, at second home visit participation in SNAP is virtually unchanged while, only 28% of women participate in WIC. Very few mothers report uptake in local food assistance programs during pregnancy (around 1%), however, enrolment in home visitation programs is reported by 6% during pregnancy. The cohort has an average Apgar score at 5 min of 9, and an average gestational age of 39 weeks.

Consistent with findings from previous literature children born to mothers enrolled federal assistance programs are more likely to be low birth weight, to have low APGAR scores small for date [77], [78]. Also consistent with Currie-Rajani's observations [80] we find that mothers of the WIC infants are younger, less likely to be married, much less educated, and more likely to smoke. They also are more likely to have complications of labor and delivery as well as more likely to be on Medicare.

3.4.2. Measures of infant cognitive and noncognitive development

Evaluation of neurodevelopmental dysfunction or delay is a central aspect of developmental psychology. The literature on standardized, developmental screening measures and associated instruments, particularly in the care of at-risk populations is vast [103]–[105]. Overall the field of developmental psychology and clinical pediatrics require that these instruments should have good concurrent and predictive properties and be readily employed in clinical settings or large studies where highly detailed assessment is not feasible.

We have chosen Bayley Scales of Infant Development which are standard measures for analyzing short to medium term outcomes of babies commonly used within the field of developmental science. The Bayley-III is a widely accepted developmental assessment instrument for children ages birth to 42 months [85]. The BSID is a global

measure of developmental status in infancy that assesses and aggregates the timely attainment of relatively crude milestones in infancy and early childhood. It is based on assumptions of a model of general intelligence that assumes that the more rapid attainment of such milestones reflects higher intellectual ability[106].

Thus, to assess cognitive outcomes at the child's CV1 (at approximately one year of age; Table 3), we used the Bayley-III [84]. The Bayley-III includes items psychometrically selected from the more comprehensive Bayley Scales of Infant Development (Bayley 2006). Internal consistency and test–retest reliability coefficients of the Bayley-III for infants' Cognitive, Receptive Communication, and Expressive Communication subtests are high to very high [107], ranging from 0.76 to 0.93 [84]. The validity of the Bayley-III, examined by determining its classification accuracy with the Bayley Scales of Infant Development, Third Edition scaled scores, showed correlations between the Bayley-III Cognitive, Receptive Communication, Expressive Communication subtests and the Bayley Scales of Infant Development, Third Edition comprehensive scales of 0.93, 0.95, and 0.95, respectively [84].

For this study, the Bayley-III was utilized to minimize infant and parent fatigue. Although the Bayley-III has five subtests, we selected the Cognitive (nonverbal), Receptive Communication, and Expressive Communication subtests as phenotypic outcomes in this study[84]. These subtests were chosen due to content similarity with other measures of cognitive development which are used later in childhood. Subtest scores are used to determine if the child's scoring is in the lowest risk or competent category, the Emerging Risk category, or the At Risk category. At 1 year of age, the Bayley-III Cognitive items focus primarily on short term visual memory, functional play, and nonverbal problem solving. Receptive Communication items include pointing to common objects or pictures of actions in a picture book, as well as responding to commands, while expressive communication items quantify emitted sound and sound combinations at 1 year of age.

A rigorous training was established to maintain Bayley-III reliability. After graduate coursework in preschool assessment and child development, the cognitive examiners attended didactic instruction on the Bayley-III. Inter-rater reliability attained

through direct observation of test administration and scoring yielded reliability coefficients equal to or greater than 0.90 on all subtests. Summary of cognitive, receptive communication and expressive communication tests for each year can be found in Tables.

3.5. Empirical Strategy

3.5.1. Overview

Our empirical objective is to isolate the causal effect of participation in WIC, SNAP on Baley scales of infant development. The challenge in answering this research question is that participation in food assistance programs is not randomly assigned. We offer an identification strategy that does not rely on this random assignment.

3.5.2. The Estimation Strategy - Panels

The analysis of how participation in federal food assistance programs affect cognitive and non-cognitive outcomes in children cannot be performed using simple comparisons between participants and non-participant women because participation is not randomly assigned. Mothers who report participation in WIC or SNAP might be systematically different in terms of both observed and unobserved characteristics compared to mothers who do not report participation. For instance, mothers who received WIC during pregnancy tend to be less educated, more likely to be of minority race, less likely to be married and more likely to be teen mothers [79], [101]. Thus, in general we expect potential outcomes of each child to differ as a function of mother's characteristics. Therefore, a selection problem arises if mothers' unobserved characteristics are correlated with both cognitive and non-cognitive outcomes in children and mothers' participation status in federal food assistance programs.

To deal with the selection problem, we relied on mother-infant fixed-effects (FE) models, which compare children outcomes among mothers who participate in federal food assistance programs and who do not participate over time. This technique uses variation in program participation status over time. In particular, it controls for

unobserved mother-infant pair characteristics, family and environmental background attributes that are time invariant. In addition, we controlled for a wide range of time-varying mother, family background characteristics, and children's characteristics.

The estimated model is

$$Y_{it} = \beta_1 F_{\mathrm{it}} + X'_{\mathrm{it}}\gamma + \alpha_i + \varepsilon_{\mathrm{it}}$$

Where $i,$ and t denote child, and survey year respectively. Y denotes the outcome of child i at first and second test respectively, F denotes mother's reported participation in WIC or SNAP at time t, X is a vector of mother-infant specific determinants of the outcome, α denotes unobservable determinants of the outcome which are specific to the mother and the child, and ε is an error term.

Our outcome, denoted Y , is a BSID test score — which is standardized within to have mean zero and standard deviation one in the entire population of children in our sample. For ease of presentation, we average standardized BSID scores for our dependent variable. Our results are not changed if instead we measure the BSID in its unstandardized scale score format. The regressor of interest F is an indicator for uptake of WIC or SNAP.

Ordinary least squares (OLS) estimation of (1) would produce biased estimates of β if $\varepsilon_{\mathrm{it}}$ were correlated with F_{it}. In other words, if there were unobservable determinants of outcome/ability correlated with unobservables. To address the potential bias due to correlation between $\varepsilon_{\mathrm{it}}$ and F_{it}, we estimate a fixed effect model relying on a rich dataset of time-varying covariates (X_{it}).

Time-varying control variables (X_{it}) include a rich set of child, caregiver, home and other contextual variables which can influence the primary developmental child outcomes including child socio-demographics, maternal characteristics, and household characteristics that may be correlated with both mothers' participation decision in food

assistance programs and children' developmental outcomes. Our choice of covariates is theory driven and heavily draws upon literature from developmental psychology [108]–[111], and economics [77]–[80], [101]. The following time varying covariates were used in the basic model: child age, child's health status, mother's maternal status, employment, knowledge of infant development, Medicaid status, and neighborhood safety. However, we used a longer covariates list to test the robustness of our results such as participation in community based programs, neighborhood quality and child's anthropometric measures.

In this model, the causal relationship between federal assistance programs uptake and child's outcomes is identified under the assumption that the differences in the uptake are exogenous to BSID scores after controlling for background characteristics. The fixed effect model uses the changes over time in the federal food assistance programs uptake within a unit of analysis as the source of variation to identify the parameter of interest. Our fixed-effects model also deals with measurement error in the outcome so long as it is caregiver family specific and time invariant.

This model does not control for the possibility that the mother-infant time-specific error term $\varepsilon_{i\mathrm{t}}$ is correlated with the participation in food assistance programs $F_{i\mathrm{t}}$. For instance, if mothers' uptake decisions over time differ in some unobserved way that cannot be controlled for and is correlated with the children' outcomes, then family fixed effects estimates will be biased. Similarly, changes in unobserved time-varying factors of the family when related to a child outcome could also confound the estimates. However, our rich dataset allows to control for all risk factors are important determinant of early developmental outcomes. We recognize that there might be some unobserved factors, but we believe that they should not affect our estimates.

One way to show the identification is to use differencing as a strategy to deal with heterogeneity parameters. Thus, consider the following model with an integrated error term

$$Y_{it} = \beta_1 F_{i\mathrm{t}} + \beta_2 L_{i\mathrm{t}} + X'_{i\mathrm{t}}\gamma + \alpha_i + \varepsilon_{i\mathrm{t}},\ \varepsilon_{i\mathrm{t}} = \varepsilon_{i\mathrm{t}-1} + u_i \ \text{ and } \ E[u_i u'_i] = \sigma^2 I_N.$$

Let Δ denote difference operator such that $\Delta X = X_t - X_{t-1}$. This implies that

$$\Delta Y_{it} = \Delta\beta_1 F_{it} + \Delta\beta_2 L_{it} + \Delta X'_{it}\gamma + u_i.$$

Thus, first differencing solves the problem of heterogeneity parameters.

3.6. Results

This section presents the estimates of federally funded nutritional programs uptake on three early childhood development outcomes: standardized receptive, and expressive communication, and cognition outcomes. In Table 3-5, each column presents the estimates of the overall effect from fixed effects estimation. The fixed effect estimates in Table 3-6 show that after controlling for observable child and mother characteristics, the effect of SNAP/WIC was statistically significant only for receptive communication outcomes.

We next performed robustness checks with additional controls and present the results in Table 3-7. Specifications 1-4 show the fixed effects estimations adding neighborhood quality, participation in community programs and the addition of anthropometric variables decreased the magnitude of the effect of interest but did not substantially changed the results.

The estimated effect of ever participation in SNAP/WIC on child's receptive communication scores is now statistically significant and it is equal to 0.32 SDs. All specifications additionally controls for family characteristics that are both time varying (child's age, health status, marital status, employment status, knowledge of infant development, neighborhood safety) and time invariant represented by the mother-infant fixed effects and year fixed effects.

We further investigate the load of time-invariant covariates on the predicted fixed effects. Table 3-8 shows that race, marital status and income group all are statistically

significant predictors of unexplained variation from time-varying controls. This justifies the use of fixed effect models.

3.7. Conclusion

In this paper, we estimated the effect of mothers' participation in the Supplementary Nutrition Assistance Program (SNAP) and the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) on early cognitive and non-cognitive developmental outcomes as measured by the Bayley Scales of Infant Development (BSID-III). In our rich data set we were able to directly identify the change in neurodevelopmental outcomes associated with changes in food programs uptake.

We found that mothers' participation in SNAP and WIC during pregnancy and in early childhood has a direct effect on cognitive and noncognitive skill formation in early age. We find that participation in food assistance programs leads to a significant increase in receptive communication as measured by Bayley scales. Our results are robust, and the inclusion of a rich set of possible confounding factors further supports the validity of the research design. Overall, our results suggest that food assistance programs improve BSID-III scores and that such programs may decrease the gaps in child ability across families of different socio-economic status.

Table 3-1 Summary statistics of BSID-III raw scores

VARIABLES	Mean at year 1	Mean at year 2
Cognitive subtest	16.97	62.31
	[2.03]	[5.82]
Receptive communication subtest	11.77	25.83
	[2.09]	[5.45]
Expressive communication subtest	12.65	29.88
	[2.09]	[5.68]
Observations	1,131	1093

Note: Data from CANDLE study. Standard deviations in parentheses.

Table 3-2 Summary of food programs uptake

VARIABLES	Mean/SD
WIC during pregnancy	0.58
	[0.49]
Supplemental programs	0.013
	[0.11]
SNAP	0.46
	[0.50]
School programs	0.24
	[0.43]
Home visitation program	0.06
	[0.23]
Observations	1,131

Note: Data from CANDLE study. Standard deviations in parentheses.

Table 3-3 Summary of infant measures

VARIABLES	Mean/SD
Gestational age (weeks)	38.82
	[1.65]
Male	0.50
	[0.50]
Birth weight (g)	3,269
	[539.2]
Birth length (cm)	50.22
	[2.99]
Birth head circumference (cm)	33.90
	[2.30]
Apgar 1 min	7.93
	[1.29]
Apgar 5 min	8.88
	[0.59]
Level of care at birth	2.09
	[0.29]
Age in months	12.76
	[1.61]
Observations	1,131

Note: Data from CANDLE study. Standard deviations in parentheses.

Table 3-4 Summary of sociodemographic measures for mothers

VARIABLES	Mean/SD
Age	26.94
	[5.40]
BMI	27.78
	[7.73]
White	0.39
	[0.49]
African American	0.62
	[0.49]
Less than high school	0.05
	[0.21]
High school diploma or GED	0.43
	[0.50]
Technical school	0.116
	[0.31]
College degree	0.25
	[0.43]
Married	0.47
	[0.49]
Living with a Partner	0.144
	[0.35]
Never married	0.35
	[0.47]
$5000-24999	0.33
	[0.47]
$25000-44999	0.16
	[0.37]
$45000-64999	0.13
	[0.33]
>$65000	0.24
	[0.42]
Tobacco use	0.09
	[0.28]
Medicaid of TennCare insurance	0.48
	[0.50]
Observations	1,131

Note: Data from CANDLE study. Standard deviations in parentheses.

Table 3-5 Overall Effect of participation in Federal Nutrition Assistance Programs (SNAP or WIC)

	Receptive	Expressive	Cognitive
WIC/SNAP	0.25**	0.10	-0.08
	[0.13]	[0.12]	[0.15]
Observations	1,226	1,226	1,226
Adj R-squared	0.01	0.00	0.00
Number of studyid	688	688	688

Note: Robust standard errors in parentheses *** p<0.01, ** p<0.05, * p<0.1.

Table 3-6 Adjusted Overall Effect of participation in Federal Nutrition Assistance Programs (SNAP or WIC)

	Receptive	Expressive	Cognitive
WIC/SNAP	0.34**	0.10	-0.09
	[0.16]	[0.14]	[0.19]
Child Age	0.01	0.01	0.01
	[0.01]	[0.01]	[0.01]
Health status	0.43***	0.11	0.21
	[0.14]	[0.13]	[0.16]
Marital status	-0.04	-0.05	-0.03
	[0.08]	[0.06]	[0.07]
Employment	-0.33***	-0.16*	-0.05
	[0.09]	[0.09]	[0.10]
Knowledge of Infant Development	0.01	0.01	0.01***
	[0.00]	[0.01]	[0.00]
Medicaid	0.00	0.07	0.05
	[0.14]	[0.12]	[0.16]
Neighborhood safety	0.16**	0.11*	0.09
	[0.07]	[0.06]	[0.09]
Observations	1,061	1,061	1,061
Adj R-squared	0.07	0.03	0.02
Number of studyid	650	650	650

Note: Robust standard errors in parentheses *** p<0.01, ** p<0.05, * p<0.1.

Table 3-7 Robustness checks more controls

	(1) Neighborhood Quality	(2) Community Programs	(3) Average Height	(4) Average Weight
DepVar: Receptive	0.34**	0.31*	0.29*	0.32*
	[0.16]	[0.16]	[0.17]	[0.17]
DepVar: Expressive	0.10	0.08	0.08	0.09
	[0.14]	[0.14]	[0.14]	[0.14]
DepVar: Cognitive	-0.08	-0.10	-0.10	0.02
	[0.19]	[0.19]	[0.20]	[0.17]
Neighborhood Quality	×	×	×	×
Community Programs		×	×	×
Average Height			×	×
Average Weight				×
Adj R-squared	0.07	0.07	0.07	0.07
F-test for extra-controls (P-val)	0.76	0.74	0.08	0.09
Time Varying Controls	×	×	×	×
Mother-Infant FE	×	×	×	×
Year FE	×	×	×	×
Sample Size	650	650	647	646

Note: Robust standard errors in parentheses *** p<0.01, ** p<0.05, * p<0.1.

Table 3-8 Regression results of predicted fixed effects on time-invariant controls

	(1) Receptive FE	(2) Expressive FE	(3) Cognitive FE
Race	0.06***	0.03***	0.001
	[0.02]	[0.01]	[0.01]
Marital Status	0.13***	0.15***	0.12***
	[0.02]	[0.01]	[0.01]
Income	-0.05***	-0.02***	-0.01
	[0.0001]	[0.0001]	[0.01]
Observations	1,574	1,574	1,574
Adj R-squared	0.23	0.19	0.17

Note: Robust standard errors in parentheses *** p<0.01, ** p<0.05, * p<0.1.

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Appendix.

Definitions of the levels of the neonatal care used in Quebec

1A: basic care + phototherapy

1B: greater or equal to 34 weeks of gestation, intravenous therapy, gavage feeding

2A:greater or equal to 32 weeks of gestation, intravenous therapy, gavage feeding

2B:greater or equal to 32 weeks of gestation, intravenous therapy, gavage feeding and ventilation via nasal passage

2B+: greater or equal to 30 weeks of gestation, intravenous therapy, gavage feeding and ventilation via nasal passage or endotracheal ventilation

3A-: greater or equal to 29 weeks of gestation, endotracheal ventilation + NO. Immediate access to all specialists.

3A: care provided to all babies regardless of their gestational age or birth weight. Endotracheal ventilation + NO. Immediate access to all specialists.

3B: level 3A care and complete access to specialists. Imaging tests carried out and interpretation of results done. Surgeries done except for severe cardiac malformations requiring extracorporeal circulation.

3C: Level 3B care + surgical repair of severe cardiac malformations requiring extracorporeal circulation.