The Influence of Socioeconomic Status On Morbidity in Late Preterm Infants

by

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Abstract:

Background/Project Description:

There is a growing interest in the contribution of late preterm (34 – 36 week gestational age (GA)) birth to neonatal morbidity and mortality. Late preterm infants have an increased incidence of both respiratory and non-respiratory complications over the first year of life. Rates of prematurity as well as morbidity/mortality in infancy are higher in lower socioeconomic status (SES) groups but how GA and SES interact is relatively unexplored.

Methods/Participant Population:

A retrospective cohort study was undertaken utilizing anonymized data housed at the Manitoba Centre for Health Policy (MCHP). A population-based cohort of infants born at 34 to 41 weeks of GA was assembled; individual and area-level income information was used to develop SES groups. Outcomes studied included diagnoses received during the birth hospitalisation, neonatal and post-neonatal admissions. Regression models were constructed to explore the effects of GA and SES as well as control for multiple perinatal variables. Appropriate approvals and safeguards for data privacy were maintained.

Results:

GA and SES exerted a gradient effect on morbidity, which persisted after controlling for multiple confounding variables. The effect of GA was strongest during the birth hospitalisation but persisted throughout the first year with increased morbidity evident with each week of decreasing GA. The detrimental association of low SES with morbidity increased in effect size throughout the first year surpassing that of GA for post-neonatal admissions. An interaction effect of maternal diabetes, respiratory morbidity and SES was suggested and merits further investigation. Neonatal stays of 3 days or longer negated the association of GA with readmission within the first 28 days; in addition shorter stay infants had the highest risks of readmission at 37 weeks as compared to the late preterm gestations.

Conclusions:

The consistent associations between poverty, prematurity and morbidity require both further study and attention. Attention to the neonatal health of both late preterm and term infants is important due to their large numbers and population impact. The added risk of poverty merits urgent and multifaceted interventions to lay the groundwork for healthy childhood and long-term success.

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Chapter 1: Introduction

There is growing recognition within the medical community of the importance of considering the determinants of health in the broader context, that there is no separation of medical and social issues in health and disease. Research from within the medical and social sciences has demonstrated the many detrimental effects of poverty on health in general,[1-5] and maternal and child health in particular.[6] Low socioeconomic status (SES) affects infants in the perinatal period via higher rates of prematurity,[6-8] stillbirth[9,10] and abnormal birth weight.[6,11] Low SES infants have higher rates of mortality,[11-13] congenital anomalies[14] and poorer health status throughout childhood,[15] with its incumbent costs. They have lower educational achievements,[15-17] with evidence that the detrimental effects of childhood poverty can extend into the next generation[18] even if the socioeconomic conditions are improved in adulthood.

Poverty is not a rare occurrence. It is estimated by Statistics Canada that almost 11.1% of Manitoba children live in poverty, and if one examines those in a high-risk group such as single parents, the risk is 26.6%. In addition, up to 30% of children experience at least one year of poverty during childhood.[19] Sporadic poverty is more common in the working poor, and can be more detrimental to health than constant poverty.[20] Poverty often coexists with other risks for poor birth outcomes such as young maternal age,[21] domestic violence,[22] less uptake of prenatal care[6] and lower maternal education.[23] Within Canada, remote areas such as Nunavut[24] and rural areas such as northern Manitoba, often have substantially higher poverty rates which are compounded by issues with timely

access to care. Poverty leads to 'living for the moment,' an inability to plan for the future including healthy lifestyle choices.[25] Estimates suggest that 5-10% of differences in child health can be attributed to neighbourhood effects, which include socioeconomic status.[26]

A similar picture of increased risk can be painted for infants born prematurely. They have higher rates of infant and neonatal mortality[27] even if only a few weeks premature. Their initial and ongoing medical care costs are higher[28,29] and they have a higher burden of respiratory[30,31] and other[32] illnesses throughout childhood. They are more likely to have ongoing developmental and educational concerns[33] or congenital anomalies.[34] When they reach adulthood they may be at higher risk of health issues such as cardiovascular disease[35] and are more likely to deliver premature infants[36] than if they had been born at term.

Prematurity and low SES are not mutually exclusive. Due to the risk factors for premature birth including both low SES itself as well as many of the factors associated with it, such as cigarette smoking,[37,38] young maternal age,[21,38,39] and chronic stress,[6,22] infants often have risk both from a medical and socio-demographic standpoint. When studies are done without considering the influence of both variables it is possible that effects due to prematurity could be falsely ascribed to low SES or vice versa. This is akin to the conflicting evidence around whether poor outcomes in teen pregnancy are due to the physiology of young maternal age or the socio-demographics of women who have children during these years.[21,22,40,41]

Prematurity, as a general term, includes all infants born at less than 37 weeks of gestation. Currently in Manitoba they represent approximately 7.7% of

all livebirths,[42] and the rate is rising: in 1989 it was 6.2%. The reasons for this worldwide increase is unclear but the bulk of the increase is in late preterm birth, that is births from 34 to 36 weeks of gestational age.[43-46] With advances in neonatal care resulting in improved survival of lower gestational age (GA) infants, most research has focused on these infants, born at less than 28 weeks of GA. On an individual basis these infants have high resource use and significant morbidity and mortality.[28] From a population standpoint however, they make up a small percentage of preterm births. Only 1-2% of births occur at less than 32 weeks, and only 0.27% of all births are born at less than 28 weeks, which is less than 50 infants per year in Manitoba. In contrast, late preterm infants make up approximately 75% of preterm infants, and 5.3% of all births, approximately 800 infants per year[47] in Manitoba. On an individual level their risks of morbidity and mortality are lower than extremely preterm infants, but on a population basis they contribute high morbidity, mortality and cost to the healthcare system.[27,28]

This thesis will focus on the late preterm population and how they compare to infants born at term, that is, 37 to 41 weeks GA. It will consider both the effects of GA and the effects of SES within one model to delineate the relative effects of each on newborn and infant morbidity. Research incorporating all risk factors for morbidity is important for decision making on all fronts. Policy makers and healthcare planners need to understand the needs of these infants and the best environment in which to provide their care. Clinicians and caregivers need to know the expected complications, both short and long term, of these infants to provide evidence based care, parent counselling and decision making around induction of delivery for fetal or maternal indications,[48] as there is evidence that

induced late preterm birth avoids stillbirth and neonatal mortality,[45,46,49,50] especially in multiple gestations. Baseline morbidity must be known in order to formulate interventions and clinical trials to improve outcomes. Strategies to decrease the late preterm birth rate where possible and to improve early outcomes are important due to the large numbers and resource usage[28,51] of this group; small improvements in morbidity per infant translate to large public health impacts. Research in this area is in keeping with recent initiatives from the March of Dimes and the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN).

This thesis utilizes a two-year birth cohort of infants born at 34-41 weeks GA in Manitoba, drawn from the data repository at the Manitoba Centre for Health Policy, to look at the effect of both variables simultaneously, preterm birth and socioeconomic status. Morbidity is examined by looking at hospital based outcomes over three different time periods: diagnoses received at birth; readmissions in the first 28 days of life, and subsequent to that until one year of age. Each of the time periods is presented in a paper that is in preparation for submission for publication. Contained within the discussions in each paper is a review of the pertinent published literature. The relative contributions of SES, GA and other perinatal variables were examined within each time period to demonstrate the unique associations of each within each time period, with and for overall trends, which are discussed in the concluding chapter.

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Chapter 2: Detailed Methodology

Data Source:

A retrospective cohort study was undertaken utilizing data housed at the Manitoba Centre for Health Policy (MCHP). The Population Health Research Data Repository (Repository) at the MCHP contains a number of different administrative datasets maintained by Manitoba Health. Personal identifying information (e.g., names, addresses) is stripped from the data sets and the Personal Health Information Number (PHIN) is scrambled at Manitoba Health prior to transfer into the Repository. The Repository contains information on almost all residents of Manitoba, with the exception of RCMP officers, inmates of federal penitentiaries and members of the Canadian Armed Forces. This study utilized data from hospital discharge abstracts, Family Services, Vital Statistics, and population registry data as well as public access Canada Census files. The results and conclusions are those of the authors and no official endorsement by the providers of the data is intended or should be inferred. Data from different datasets was linked for this analysis using a scrambled PHIN. All linkages were made via computerized files. Postal codes were required to link data, but presentation of data at the individual postal code level was not done. Appropriate approvals were obtained from the custodians of all information sources in addition to the University of Manitoba Health Research Ethics Board and the Health Information Privacy Committee of Manitoba.

Study Population and Study Period:

The study population included all infants born in the fiscal years 2004/2005 and 2005/2006. The cohort included all infants born at 34 – 41 completed weeks gestation in these years who remained in Manitoba until one year chronological age. Information on birth outcomes and birth hospitalisation was taken from the infant's hospital record. To calculate mortality and readmission rates for all infants, hospital data up to 2006/07 was used. The infant's record was linked to the maternal hospital and prenatal record for extraction of pregnancy related variables. Power analysis using currently published readmission and morbidity rates[1-13] for late preterm infants was undertaken. Two years of data, or an initial birth pool of 28 000 was determined adequate to detect a small but clinically significant difference (OR 1.2) with 80% power.

The initial dataset contained 25 834 newborn records that were matched with population registry (22 unmatched) and maternal health records (2 unmatched) successfully for 25 810 infants. Of these, 436 moved before their first birthday and 62 were missing essential demographic data (birth weight, GA or income data) and were removed from the analysis, resulting in a final cohort of 25312 infants. Income and GA distribution of those infants who moved did not differ significantly from those retained in the sample (see Table 1). The dataset of admissions (after initial birth hospitalization) initially contained 4 467 records. These were further classified into 3 993 discrete hospitalizations, after inter-hospital transfers were merged into one admission. Infants classified as boarder infants, that is, those infants admitted to accompany another requiring care, usually their mother, not due to their own illness, were not included in the

analysis, they constituted 323 of the admission episodes, leaving a total of 3 670 admission episodes in infants up to 365 days of age. Counts of admissions were generated from these records and merged to the mother-infant pair records.

Table 1: Characteristics of infants who moved at less than 365 days of age with chi-square statistic for comparison to retained cohort

SES group	low	middle	high	unknown					chi-square
	136	143	110	47					p=0.19
	31.2%	32.8%	25.2%	10.8%					
GA (weeks)	34	35	36	37	38	39	40	41	chi-square
	6	10	11	33	68	116	124	68	p=0.96
	1.4%	2.3%	2.5%	7.6%	15.6%	26.6%	28.4%	15.6%	
preterm	6.2%								

Predictor Variables:

Socioeconomic status:

There are multiple methods used in the literature to measure socioeconomic status (SES). This analysis utilized two separate measures. The first SES variable was an individual level measure of SES, based on receipt of provincial income assistance by the mother in the month of delivery. Information on income assistance receipt was taken from the Manitoba Family Services and Consumer Affairs, Employment and Income Assistance database. Within Manitoba there are both provincial and national income assistance programs, with the national program mostly applicable to First Nations individuals living on reserve. The data at MCHP only contain information on recipients of the provincial income assistance program. The second measure of SES used area-level income derived from the Statistics Canada Census data. Mean household income in the area level was applied to individuals using 6-digit postal codes and then individuals were assigned to an income quintile, with each quintile

containing approximately 20% of the population. Quintiles were ranked from poorest to wealthiest, with rural and urban quintiles generated separately. To maintain group size and to avoid multiple between-class comparisons, SES groups were constructed from a combination of these two SES variables. Infants coded as receiving income assistance were classified into the lowest SES grouping. Of those not on income assistance, quintile 1 was also included in the lowest SES group; the next group (middle) consisted of income quintiles 2 and 3; and the final group (highest) contained income quintiles 4-5. Rural and urban quintiles were combined for analysis; a separate urban/rural variable was entered into the model in order to adjust for its influence. Other planned markers of SES were removed from the models due to their confounding effect on outcomes or unacceptable correlation with other variables.

The utilization of area level income data to study the effect of SES on individual health outcomes has been validated previously[14] in a study by Mustard et al. They compared the effect of individual household income versus area-level income on various health outcomes. Similar odds ratios for the effect of SES on injury admissions were seen, and for respiratory admissions in children, a greater effect of neighbourhood was seen than for individual income. Fertility rates were similarly affected by SES regardless of which indicator was used. There is a theoretical risk of less specificity in rural areas, but this was not borne out in the above study. Multiple administrative databases within Canada have been used to study both socioeconomic status and hospitalisation and have acceptable levels of accuracy when compared to other methods.[15, 16] Studies utilizing area-level data in these systems compare favourably to American studies utilizing maternal

education from birth certificate data, and the large Scandinavian databases as discussed in the results sections of this thesis.

Maternal Variables:

Maternal variables available from the hospital record, including the discharge abstract and prenatal record, included maternal age (years), maternal diabetes (any type) and parity. There was no distinction made between types of diabetes, as insufficient clinical data on the maternal history is available from the database. The variable 'induced delivery' included those infants delivered either via caesarean section without any labour, or following induction of labour (regardless of ultimate mode of delivery). This was assembled using ICD10[17] and CCI[18] codes from the discharge abstract. This variable is meant to represent those infants who did not deliver following spontaneous start of labour, and to separate out iatrogenic preterm delivery for fetal or maternal indications from spontaneous preterm labour. This group would not include those infants induced following spontaneous rupture of membranes prior to labour. Caesarean section type, elective or emergency, is not well captured in the database and thus was not examined.

Newborn Variables:

Infant gender, delivery type, single or multiple gestation, birth date, 5-minute Apgar score, birth weight, hospital of birth and postal code were taken from the newborn record. All postal codes outside of Winnipeg and Brandon were considered rural. Gestational age (GA) was taken from the maternal database, and is based on menstrual or ultrasound dates where available. If the clinical

impression after delivery differed dramatically, the responsible physician recorded the best estimate. Weight for GA was generated from birth weight, sex and GA using current growth standards.[19] Infants were small for GA (SGA) if they were less than the 10th percentile and large for GA (LGA) if above the 90th percentile. Infants without sufficient information to establish their size for GA were excluded from the analysis. Any infant receiving a diagnostic code from the significant congenital anomalies set (see Appendix 1), over the first year was classified as having a congenital anomaly (CA) in the analyses. Significant congenital anomalies were those expected to cause significant issues with growth and development such as chromosomal and developmental anomalies, cardiac and gastro-intestinal defects and inborn errors of metabolism. They did not include diagnoses such as birthmarks, or easily repaired anomalies such as inguinal hernia or hypospadias. The infants experiencing complications from a CA during their birth hospitalisation or being subsequently hospitalised with a CA code as their most responsible diagnosis form a subset of all infants with a CA. Breastfeeding status was taken from the birth record, and codes grouped to generate a binomial variable. Those records indicating exclusive, or mixed feeding were classified as ‘any breastfeeding’, with those infants recorded as NPO or formula as ‘no breastfeeding’. Infants who received positive pressure ventilation (PPV), intubation, chest compressions or medications for resuscitation at birth were coded as receiving resuscitation. Infants receiving only Naloxone or only oxygen were not considered to have received resuscitation.

Data Analysis:

Morbidity was examined by looking at diagnoses received during the birth hospitalisation and during hospital admissions over the first year of life. Mortality and stillbirth rates are reported for comparison but this study is not powered to detect between-group differences thus no statistical analysis was done. The primary predictors of interest are GA and SES. In the univariate analyses between-group differences were tested using a Chi-square or Cochran Armitage test for trend. To delineate the relative contributions of GA and SES after controlling for confounding variables, the outcomes were analyzed using logistic regression. All data handling and statistical analysis were conducted in a secured environment using SAS software version 9.1 of the SAS System for Unix[20]

It is unknown if there is a differential effect of SES depending on GA and thus in the regression models it was entered as an interaction and retained as such if significant. It is unknown if the sample size is powered to look at an interaction effect as there is no published data in this area. A p-value of <0.05 is taken as significant in all tests. Data are presented in text, tabular or chart form. No child, parent, patient, or physician identifiable data are presented. Groupings that resulted in less than 6 individuals were suppressed. No individual level information is published; all data are presented as rates within a defined group.

Outcome measures:

Overall Characteristics:

The distribution of select independent variables was reported by GA and SES, to examine their distribution in the cohort, to aid in planning of the final analysis.

Mortality:

Infant and neonatal mortality was ascertained using Vital Statistics and Registry data. Stillbirth rates are reported, but all totals in descriptive and statistical analyses are for livebirths only.

Newborn Resource Usage:

Length of stay and need for ventilation or phototherapy were taken from the newborn record. Level of care required was analysed using Special Care Unit Admission as the variable. Normal nursery care, including combined care postpartum wards, are designated Level I. Level II and Level III care, combined into Special Care Unit (SCU) admission in the discharge database, is for infants requiring monitoring or advanced nursing care (Level II) or respiratory support (Level III). Admission criteria and procedures for admitting infants to Level II or III nurseries differ from centre to centre, and in some centres both levels of care would be provided in one geographic location. Due to differing coding practices it is not consistently possible to separate level II from level III admissions and thus they were analyzed as one group, under the title of special care unit (SCU) admission. There are three Level II/III nurseries in Manitoba, two in Winnipeg and

one in Brandon, with a Level II nursery in Thompson. All other delivery centres in Manitoba provide only Level I care.

Several variables from the birth hospitalisation study were utilized during the follow-up studies of neonatal and post neonatal admissions as predictor variables. These include jaundice in the newborn period, an SCU stay at birth, a birth morbidity diagnosis and need for ventilation. Also included was short stay at birth, defined as two days or less. Due to time of birth and coding of a new day of stay at 24:00 hours this does not translate directly to 48 hours; some infants discharged at less than 48 hours of age could be three day stays, or infants staying just over 24 hours could be coded as a 2 day stay.

Morbidity:

Morbidity was assessed using diagnoses from the initial birth hospitalisation abstract and from hospital admissions over the first year of life. Three separate sets of outcomes were examined and are described in the three papers following this introductory methods section.

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Chapter 3: Characteristics of the Study Cohort

The overall rate of preterm delivery within the study cohort of infants live born at 34 to 41 weeks was 6.1% (n=1534) with 66.4% (n=1019) of those being spontaneous preterm deliveries. The spontaneous delivery group includes those infants induced following spontaneous rupture of the fetal membranes.

Mortality:

Within the cohort there were 34 deaths in the neonatal period (up to 28 days of age), with 47.1% (n=16) of these in preterm infants. Approximately two thirds of deaths within each GA cohort were due to congenital anomalies. If one looks at the SES distribution, 44.1% (n=15) were from the lowest SES group. For total infant mortality there were 64 deaths, with 42.2% (n=27) in low SES infants. The numbers for preterm infants were suppressed. There were 97 stillbirths delivered at 34 to 41 weeks within the time period under study, with 23.7% (n=23) of these delivered preterm.

Morbidity:

When the data were examined by GA (Table 1), significant between-group differences were seen. For all variables there were significant differences between infants of different gestations ($p<0.01$). Preterm infants were more likely to be born to a mother over 34 years of age compared to the rest of the maternal age groups, OR=1.35 [1.17-1.55]. There were 268 matched sets of twins, and one set of triplets, with seven infants coded as twins having no matching twin found; thus 2.2% of the infants were a product of multiple gestation. The ‘single’

twins could represent in-utero death, stillbirth or coding error in the other twin. The incidence of multiple births fell dramatically as gestation increased. The incidence of induced delivery was low in 34-week infants, relatively stable across the 35-38 week range, lower again at 39 – 40 weeks, with an upward trend at 41 weeks. The caesarean section (CS) rate also fell as GA increased up to term, then started to rise at 41 weeks, as expected with the accompanying inductions for post dates pregnancies and fetal distress. The overall incidence of maternal diabetes in this cohort was 4.8% with overrepresentation in the preterm infant, especially in mothers of infants at 35-36 weeks. The percent of mothers with low socioeconomic status (lowest income quintile combined with receipt of income assistance) was higher in the preterm infants.

The overall incidence of congenital anomalies (diagnosed over the first year of life) was 2.5% with overrepresentation again in the preterm infant as many of these anomalies or their etiologic factors predispose to preterm delivery. The incidence of 'any morbidity' diagnosis during birth hospitalization, discussed in Chapter 4, demonstrated a steady decline as GA increased without a clear divide between preterm and term. Morbidity started to trend upwards again at 41 weeks as post-maturity complications started to occur. Males were overrepresented in preterm infants, and birth weight increased with GA. Length of stay was non-normally distributed with outliers in all groups. The median length of stay was substantially longer in 34 week infants and then decreased to the median of 2 days at 37 weeks and above.

Table 1: Characteristics of study population by GA at birth and selected maternal and neonatal variables

GA	34	35	36	37	38	39	40	41	
n	276	457	801	1780	4189	6535	7218	4056	
Maternal Characteristics									
maternal age group, years									
<19	5.8	3.5	4.2	4.9	4.4	5.4	5.1	5.5	
19-34	80.4	81.2	78.0	79.0	80.5	82.2	83.5	83.3	
>34	13.8	15.3	17.7	16.1	15.1	12.4	11.4	11.2	
primiparous, %	44.2	39.6	36.6	35.7	32.5	35.1	39.4	46.8	
CS, %	35.9	33.7	29.0	24.9	30.1	21.2	13.9	17.2	
induced delivery	26.8	35.2	35.0	33.7	34.8	22.1	16.4	39.1	
multiple birth	23.6	21.9	11.7	8.0	2.7	0.3	0.2	0.0	
maternal diabetes	7.6	12.0	17.2	10.1	8.5	3.8	2.4	0.8	
low SES	35.9	37.2	39.3	36.8	33.6	31.8	31.2	30.4	
Newborn Characteristics									
male, %	58.0	55.4	54.2	51.7	53.0	49.6	50.1	51.9	
mean BW, grams (SD)	2377 (460)	2640 (534)	2936 (530)	3143 (480)	3358 (479)	3496 (459)	3656 (463)	3774 (469)	
BW range	1184-3902	1216-4599	1420-5160	1172-5305	1610-6440	1703-6457	1349-5589	1438-5795	
median LOS (range)	13 (1-90)	6 (1-66)	3 (1-71)	2 (1-103)	2 (1-168)	2 (1-93)	2 (1-55)	2 (1-42)	
any neonatal morbidity, %	85.5	62.4	45.3	23.4	17.6	11.6	11.6	12.1	
major congenital anomaly, %	10.1	5.7	5.6	3.2	3.1	2.1	1.7	2.1	
short stay, %	7.3	11.8	28.2	56.7	61.3	70.9	74.9	70.6	

Please see text for description of variables, CS=cesarean section, SES=socioeconomic status, BW=birthweight, LOS=length of stay

Trends across income groups are shown in Table 2. The proportion of young mothers decreased as income increased, with a reverse trend in the older mothers. Primiparity was lower in the lower income groups. Both the CS and multiple birth rates increased with increasing income. There was no significant difference in the gender distribution across income, and a small but statistically significant difference in birth weight (9-20g) across the income strata, not adjusted for GA or other factors. Infants born to mothers in the lower socioeconomic groups were more likely to have a major congenital anomaly, suffer a neonatal morbidity and be premature. There was a higher percent of maternal diabetes with over twice the rate in the lowest income group versus the highest.

Table 2: Characteristics of study population by SES and selected maternal and newborn characteristics

SES group	lowest	middle	highest	chi-sq
n	8203	8854	8255	
Maternal Characteristics				
maternal age group, yrs <19	10.3	3.3	1.7	p<0.0001
19-34	81.6	83.7	80.8	p<0.0001
>34	8.1	12.9	17.5	p<0.0001
primiparous, %	33.3	40.2	40.6	p<0.0001
CS, %	17.5	21.9	23.0	p<0.0001
maternal diabetes	7.2	4.2	3.0	p<0.0001
induced delivery	25.5	27.9	26.9	p=0.0014
multiple birth	1.7	2.0	2.8	p<0.0001
rural	45.8	44.5	42.3	p<0.0001
Newborn Characteristics				
male, %	51.3	51.4	51.0	p=0.7066
mean BW, grams (SD)	3482 (554)	3505 (534)	3492 (526)	
BW range	1216-6208	1172-6457	1331-5746	
median LOS (range)	2 (1-103)	2 (1-168)	2 (1-51)	
premature	7.1	5.4	5.7	p=0.0001
any neonatal morbidity, %	17.7	17.2	14.0	p<0.0001
major congenital anomaly, %	2.8	2.6	2.1	p=0.0046
short stay, %	67.0	65.3	66.6	p=0.0559

BW=birthweight, CS=cesarean section, LOS=length of stay, SES=socioeconomic status

Discussion:

There are several interesting patterns revealed in this cohort that underline the need for further detailed examination. The separation of infants born following spontaneous preterm labour from those delivered prematurely for maternal or fetal indications is difficult in administrative data, but is an important distinction. Increased delivery of late preterm infants for medical indications has reduced the stillbirth rate. [1-4] Our proportion of spontaneous preterm delivery at 66.4% is slightly lower than the most recent Manitoba data at 70%,[5] but our study does not include more preterm infants. In addition our study considered infants induced for preterm rupture of the membranes to be spontaneous; these infants would be considered an induction in the Manitoba study above. This variation could be due to our lack of inclusion of infants born at less than 34 weeks, change in coding practices or due to changes over time. The reported variation in the literature is from 30% to over 90% depending on definition and local practice.[2,6-9] The induced delivery variable in this study includes inductions of labour and all types of CS in a non-labouring patient, emergency and elective, but not those induced following premature rupture of membranes. Whether infants who are induced following spontaneous rupture of membranes are coded as spontaneous or induced varies from study to study. Maternal diabetes is a risk factor for stillbirth[10, 11] leading to induction and delivery at these gestations, as reflected in the GA pattern and induction rates of mothers with diabetes. The incidence of multiple gestation fell by almost 300% from 34 to 37 weeks and even further at 38 weeks and above. An increase in multiple births, associated with the increased

use of reproductive technologies and advancing maternal age, is one of the reasons behind the increasing late preterm birth rate.[1,12] Older mothers in this sample were more likely to be of higher SES and deliver a preterm infant.

Higher preterm birth is not limited to older mothers; despite being younger overall, low SES mothers are more likely to have preterm infants, maternal diabetes, neonatal morbidity and a congenital anomaly, keeping with the published literature.[13-18] In contrast to the association of LBW infants with low SES found in the literature,[18,19] the birth weight difference in this sample was very small, only 10g between the lowest and highest SES groups, not adjusted for any other differences. The lack of difference in birth weight across SES could be due to the prevalence of maternal diabetes in low SES mothers, which can be associated with macrosomia. Of note also are the extremes in birth weight in each GA group, highlighting the importance of using both weight and GA when discussing outcomes, as infants considered low birth weight (<2500g) and high birth weight (>4000g) are represented in all GA categories. The multiple between-group differences seen here underline the importance of controlling for these variables in further analyses.

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Chapter 4: The influence of SES on birth hospitalisation morbidity

There is a growing interest in the contribution of late preterm (34 – 36 week gestational age (GA)) birth to neonatal morbidity and mortality. Currently these infants are often included with term (37 – 41 weeks GA) infants in outcomes analyses. As research accumulates specific to these infants it becomes more obvious that it is to their disservice to assume they are equivalent to term. What remains unclear and as yet largely unexplored is the contribution of socioeconomic status to the outcomes for these late preterm infants.

The focus in the past, on respiratory maturity as the benchmark to establish equivalence to term, is overly simplistic and ignores the other issues prevalent in this population. Held as the most important complication of preterm delivery, respiratory distress syndrome (RDS) has a relatively low absolute risk at late preterm and term gestations, reported in the literature at 7-15% at 34 weeks to 0-5% at 36 weeks. Arguments against considering only respiratory maturity as important accumulate as physiology,[1-3] spectrum of disease[4-7] and clinical care required[8-10] differ in many ways, even in an infant with 'mature' lungs. Late preterm infants are more likely than term infants to have respiratory distress due to other etiologies as well, need extra care at delivery and need admission to special care nurseries.[3,6,9,11-14] Often overlooked in the late preterm infant is the significant incidence of other complications associated with prematurity including poor feeding, hypoglycemia, temperature instability and apnea.[4,9,10,15,16] In addition whilst absolute mortality is low, Canadian data demonstrate a relative risk compared to term infants of 1.9 - 7.9 times for various categories of death,

both infant and neonatal.[14,17] Whilst not the topic of this paper, late preterm infants remain at risk throughout infancy and childhood for increased hospital admissions, health care needs and developmental issues.

Preterm delivery rates are increasing, with a disproportionately high increase in the late preterm cohort.[18-20] Rates of prematurity as well as neonatal morbidity/mortality are higher in lower SES groups.[11,18,21-26] Strategies to decrease the preterm birth rate where possible and to provide comprehensive evidence based care to these infants are important due to their large numbers and resource usage.[27,28] Some infants are delivered preterm due to fetal or maternal complications, and understanding the complications, both short and long term, associated with delivery is important to make informed decisions.[29] There is evidence that induced late preterm birth avoids stillbirth and neonatal mortality,[20, 30-32] especially in multiple gestations. Small improvements in morbidity per infant translate to large public health impacts. If SES compounds the risks of prematurity it is especially important that its effects are understood and programs put in place to mitigate these wherever possible. This study will attempt to characterize this relationship as it pertains to the late preterm infant specifically, to determine how SES modifies the morbidities experienced.

Methods:

A retrospective cohort study was undertaken utilizing data housed at the Manitoba Centre for Health Policy (MCHP). The Population Health Research Data Repository (Repository) at the MCHP contains a number of anonymized administrative datasets maintained by Manitoba Health. This study utilized data

from hospital discharge abstracts, Vital Statistics, and population registry data as well as public access Canada census files and data from Family Services. The results and conclusions are those of the authors and no official endorsement by the providers of the data is intended or should be inferred. The Repository contains information on almost all residents of Manitoba, with the exception of RCMP officers, inmates of federal penitentiaries and members of the Canadian Armed Forces. Appropriate approvals were obtained from the custodians of all information sources in addition to the University of Manitoba Health Research Ethics Board and the Health Information Privacy Committee of Manitoba.

The cohort includes all infants born at 34 – 41 completed weeks gestation during the fiscal years 2004/2005 to 2005/2006, who remained in Manitoba until their first year birthday. It also includes the linked maternal file for extraction of pregnancy related variables. The initial dataset contained 25 834 newborn records that were matched with population registry (22 unmatched) and maternal health records (2 unmatched) successfully for 25 810 infants. Of these, 436 moved before their first birthday and 62 were missing essential demographic data (birth weight, GA or income data) and were removed from the analysis, thus resulting in a final cohort of 25 312 infants. Income and gestational age distribution of those infants who moved did not differ significantly from those retained in the sample (see Chapter 2).

Two different variables were used to assign infants to an SES group using maternal data. An individual level variable, receipt of provincial income assistance by the mother in the month of delivery, placed an infant in the lowest

SES group. Area-level income information on average household income from Canada Census data was aggregated at the dissemination area level (approximately 400 persons) and grouped into population quintiles. Income quintiles were used to place the infants not on income assistance into one of the three groups. Infants in income quintile 1 were placed in the lowest group along with the income assistance recipients; quintiles 2 and 3 were placed in the middle group, and quintiles 4 and 5 in the highest group. GA was taken from the hospital record, which was based on menstrual dates or ultrasound dating unless the clinical estimate at delivery differed in the opinion of the physician of record.

The remaining predictor variables were taken from the hospital abstract with some codes grouped to generate composite variables, as described below. Size for gestational age was generated from birth weight, gestational age, and sex, and grouped according to growth percentiles.[33] Need for resuscitation was defined as receiving positive pressure ventilation, chest compressions or drugs for resuscitation at delivery. The variable 'induced delivery' was assembled using ICD 10[34] and CCI[35] codes from the maternal record to include those infants who either had a caesarean section without any labour or an induction of labour (regardless of ultimate mode of delivery). It is meant to represent those infants who did not deliver following spontaneous start of labour, and to separate out iatrogenic preterm delivery for fetal or maternal indications from spontaneous preterm labour. An infant receiving at any time a code from the significant congenital anomaly set (Appendix 1) is defined as having a congenital anomaly in the analysis.

The outcome was infant morbidity during birth hospitalisation, and was divided into groups for analysis as defined below. All diagnosis codes from the hospital discharge abstract were included, thus infants could be represented in multiple groups. Please see Appendix 1 for codes utilized. The groupings were:

1) **Respiratory Distress Syndrome (RDS):** if recorded as the reason for respiratory symptoms on the discharge abstract.
2) **Other complications of prematurity**: Apnea, hypoglycemia, temperature instability and poor feeding
3) **Jaundice:** clinically diagnosed
4) **Other Respiratory morbidity**: All other causes of respiratory distress in the newborn including transient tachypnea (TTN), pneumonia, aspiration, persistent pulmonary hypertension (PPHN), air leak syndromes, pulmonary hemorrhage, aspiration (including meconium) or respiratory arrest.
5) **Other major morbidity**: All other significant (i.e., affecting length or stay or care required) illnesses and conditions coded in the newborn period not captured in the congenital anomalies grouping below, or in the other groups already described.
6) **Congenital and chromosomal anomalies**: Major congenital anomalies expected to be symptomatic over the first year of life.
7) **Resource Utilization:** Admission to a Level II/III nursery (Special Care Nursery, SCU), need for resuscitation at birth, need for ventilation or

receipt of phototherapy and average LOS were used to indicate resource use.

Regression models were constructed to control for the effect of other perinatal variables expected to be associated with the outcomes. Models were not run for congenital and chromosomal anomalies, need for resuscitation at birth, or length of stay. To most clearly illustrate the impact of gestational age, and to examine the possible significance of the upward trend in morbidity at 41 weeks, GA was entered as a classed variable with 39-40 weeks GA as the reference group for all but the RDS and need for ventilation models. Models run initially with each week GA separately demonstrated no significant differences between 39 and 40 week infants, thus they were combined to maintain sample size. Dichotomous medical variables were parity (primiparous or multiparous), maternal diabetes (any type), 'induced delivery', multiple birth, caesarean section (CS) delivery, male sex, SGA, LGA, congenital anomaly (diagnosed over the first year of life), rural residence, need for resuscitation at birth and infant feeding (any breastfeeding vs. no breastfeeding). Maternal age was entered as a categorical variable with three groups (<19, 19-34 and >35 years). The 19-34 year age group was used as the reference.

Socioeconomic status was analyzed using the income groups previously described, with highest as the reference. Logistic regression models were initially run with an interaction variable for SES and GA; the interaction was dropped if not significant. In the RDS and need for ventilation models no interaction term was included, and income was entered as two groups, low versus middle/high

combined; this is due to sample size constraints. All other variables were retained. Significance was set at $p<0.05$. All data handling and statistical analysis was done using SAS version 9.1 for Unix.[36]

Results:

For characteristics of the sample by GA and SES please see Tables 1-2. Of the 25 312 infants in the birth cohort, 6.1% (n=1524) were born preterm at 34 to 36 weeks GA.

Table 1: Characteristics of study population by GA at birth and selected maternal and neonatal variables

GA	34	35	36	37	38	39	40	41
n	276	457	801	1780	4189	6535	7218	4056
Maternal Characteristics								
maternal age group, years								
<19	5.8	3.5	4.2	4.9	4.4	5.4	5.1	5.5
19-34	80.4	81.2	78.0	79.0	80.5	82.2	83.5	83.3
>34	13.8	15.3	17.7	16.1	15.1	12.4	11.4	11.2
primiparous, %	44.2	39.6	36.6	35.7	32.5	35.1	39.4	46.8
CS, %	35.9	33.7	29.0	24.9	30.1	21.2	13.9	17.2
induced delivery	26.8	35.2	35.0	33.7	34.8	22.1	16.4	39.1
multiple birth	23.6	21.9	11.7	8.0	2.7	0.3	0.2	0.0
maternal diabetes	7.6	12.0	17.2	10.1	8.5	3.8	2.4	0.8
low SES	35.9	37.2	39.3	36.8	33.6	31.8	31.2	30.4
Newborn Characteristics								
male, %	58.0	55.4	54.2	51.7	53.0	49.6	50.1	51.9
mean BW, grams (SD)	2377 (460)	2640 (534)	2936 (530)	3143 (480)	3358 (479)	3496 (459)	3656 (463)	3774 (469)
BW range	1184-3902	1216-4599	1420-5160	1172-5305	1610-6440	1703-6457	1349-5589	1438-5795
median LOS (range)	13 (1-90)	6 (1-66)	3 (1-71)	2 (1-103)	2 (1-168)	2 (1-93)	2 (1-55)	2 (1-42)
any neonatal morbidity, %	85.5	62.4	45.3	23.4	17.6	11.6	11.6	12.1
major congenital anomaly, %	10.1	5.7	5.6	3.2	3.1	2.1	1.7	2.1
short stay, %	7.3	11.8	28.2	56.7	61.3	70.9	74.9	70.6

Please see text for description of variables, CS=cesarean section, SES=socioeconomic status, BW=birthweight, LOS=length of stay

Table 2: Characteristics of study population by SES and selected maternal and newborn characteristics

SES group	lowest	middle	highest	chi-sq
n	8203	8854	8255	
Maternal Characteristics				
maternal age group, yrs <19	10.3	3.3	1.7	p<0.0001
19-34	81.6	83.7	80.8	p<0.0001
>34	8.1	12.9	17.5	p<0.0001
primiparous, %	33.3	40.2	40.6	p<0.0001
CS, %	17.5	21.9	23.0	p<0.0001
maternal diabetes	7.2	4.2	3.0	p<0.0001
induced delivery	25.5	27.9	26.9	p=0.0014
multiple birth	1.7	2.0	2.8	p<0.0001
rural	45.8	44.5	42.3	p<0.0001
Newborn Characteristics				
male, %	51.3	51.4	51.0	p=0.7066
mean BW, grams (SD)	3482 (554)	3505 (534)	3492 (526)	
BW range	1216-6208	1172-6457	1331-5746	
median LOS (range)	2 (1-103)	2 (1-168)	2 (1-51)	
premature	7.1	5.4	5.7	p=0.0001
any neonatal morbidity, %	17.7	17.2	14.0	p<0.0001
major congenital anomaly, %	2.8	2.6	2.1	p=0.0046
short stay, %	67.0	65.3	66.6	p=0.0559

BW=birthweight, CS=cesarean section, LOS=length of stay, SES=socioeconomic status

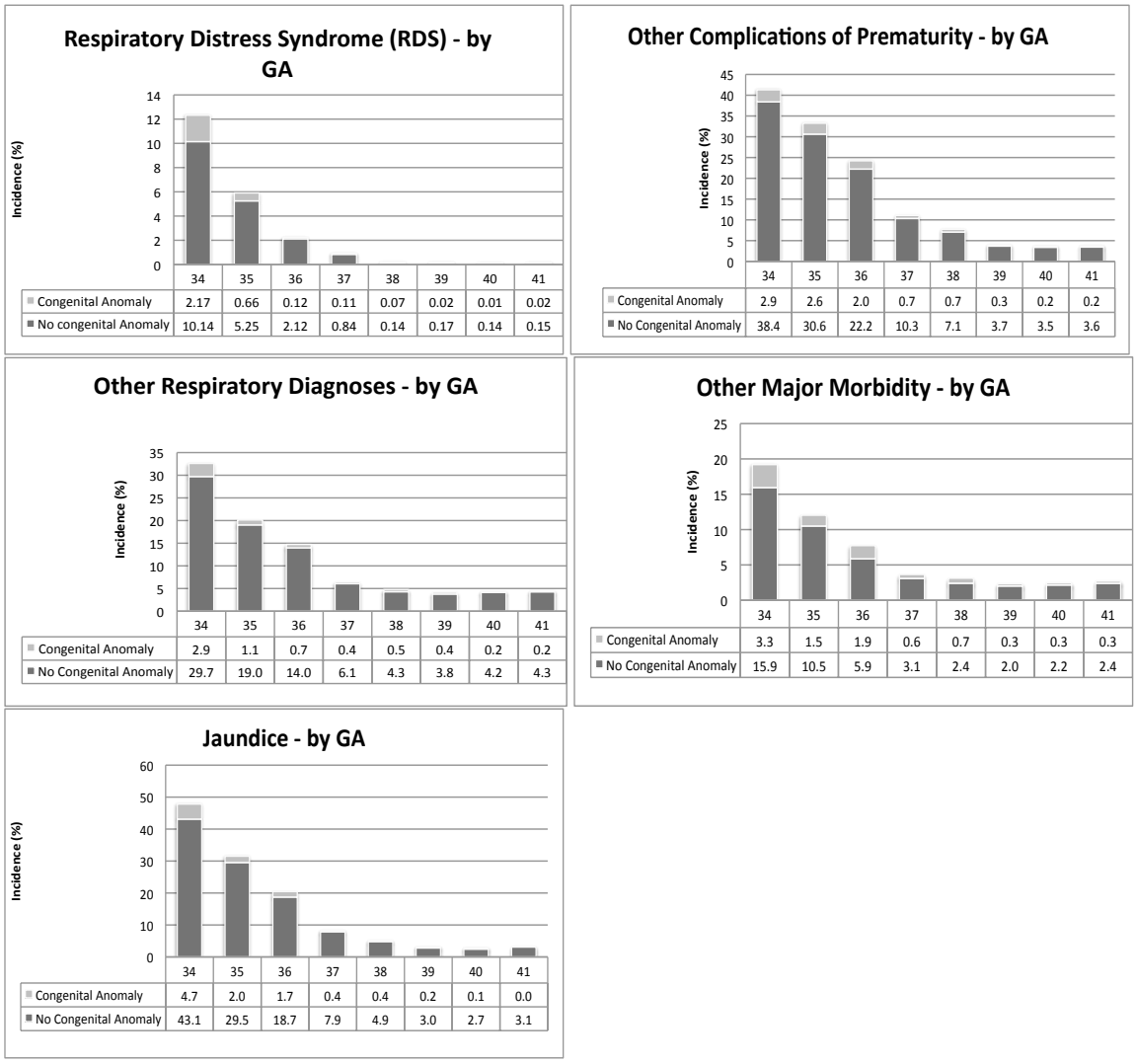
Diagnoses Received:

Univariate Analysis by Gestational Age (Figures 1-2):

The overall trend was of decreasing incidence of morbidity as gestational age increased up to 40 weeks, for all outcome groups. In the 41 week cohort some outcome groups demonstrated a slight upward trend. While the absolute prevalence of RDS was low in late preterm infants (5.2%), it is markedly higher compared to term infants(0.24%), OR=23 [16.7-22.5]. 'Other respiratory morbidity' was also more common in the late preterm infant, 19.6% vs. 4.6%, OR=5.1 [4.4-5.8]. There is imprecision clinically in the distinction between RDS and other newborn respiratory distress, especially transient tachypnea (TTN), but even if one combines these two respiratory diagnoses the incidence of 18.6 vs.

2.7% generates an OR=8.4 [7.2-9.7] for either of these two diagnoses in the late preterm infant. None of these OR however are adjusted for other risks.

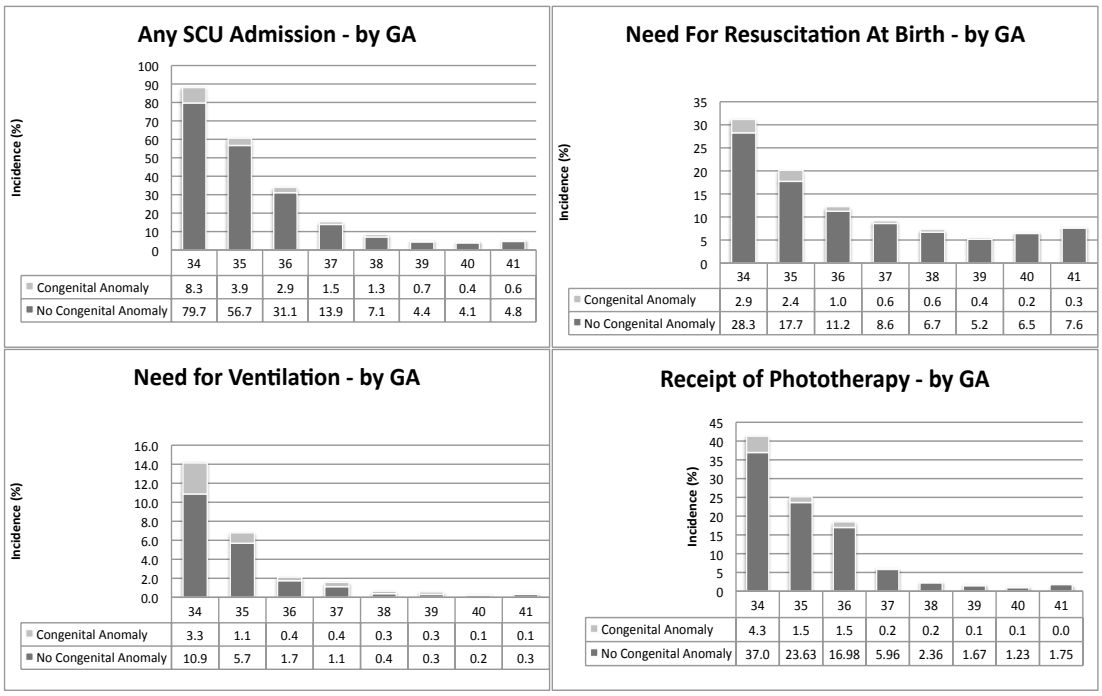
Figure 1: Percentage of infants with a diagnosis in each outcome group, by GA and presence of congenital anomalies



While respiratory outcomes are often the most focused upon, the 'other complications of prematurity' demonstrate a steeper gradient across gestational age, a greater than tenfold decrease from 34 to 39 weeks GA, and levelling off at 39-40 weeks. The 'other major morbidity' group also showed higher incidence at

lower gestations, a plateau at 39-40 weeks and the beginnings of an upward trend at 41 weeks. The prevalence of jaundice using either the diagnosis or receipt of phototherapy fell dramatically with increasing GA, 14-20x depending on definition, with the most marked drop-off occurring at 37-38 weeks.

Figure 2: Resource utilization, by indicator, GA and presence of congenital anomaly



Resource utilization and level of care required also decreased with increasing gestational age with a slight increase from 40-41 weeks GA. A substantial proportion of late preterm infants without congenital anomalies (11.2-28.3%) required resuscitation at birth compared to term infants without anomalies (5.2-8.6%). Need for ongoing ventilation demonstrates a higher contribution by infants with congenital anomalies, more of a threshold effect at 35-36 weeks, and less of an increase at the 40-41 week mark. Admission to an SCU showed an intermediate pattern between these two, with 88.0% of 34 week infants admitted,

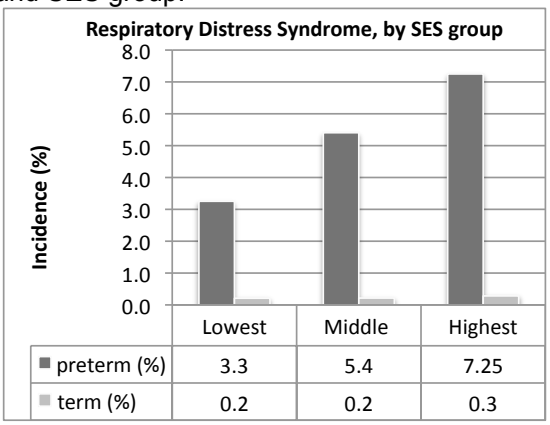
a gradual decrease with less of a threshold at 36-37 weeks and a relatively stable incidence in infants at or greater than 38 weeks GA. Notably there is still a significant proportion, 34.0% at 36 and 15.3% at 37 weeks, requiring an increased level of nursing care.

Univariate Analysis by Socioeconomic Status (Figures 3-4):

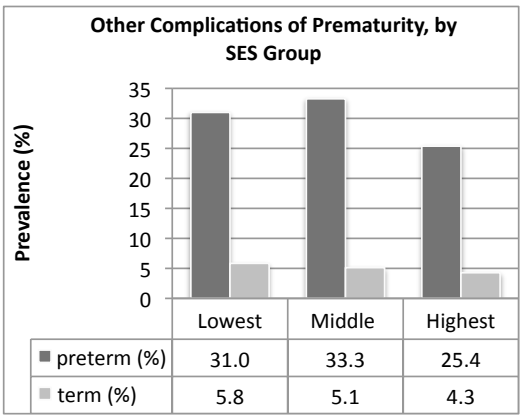
When looking at the data from a socioeconomic standpoint fewer trends are seen. In the preterm infants there were few significant between-group differences. The most obvious was a higher percentage of infants with RDS, as socioeconomic status increased, this trend was also seen in 'need for ventilation'. This was irrespective of congenital anomalies with almost triple the incidence at the highest income level over the lowest. Inspection of the graphs for each of the other outcomes reveals no patterns in the preterm infant.

In the term infant however patterns emerge. For RDS numbers were too small to examine. No linear trends but significant between-group differences were seen for the other respiratory morbidity group, jaundice and the other major morbidity group, all at $p<0.0001$. The percent of infants with these outcomes was lowest in the highest income group but highest in the middle income group, with the lowest income group intermediate between the two. A linear trend demonstrating less morbidity as income increased was seen in other complications of prematurity group ($p<0.0001$), receipt of phototherapy ($p=0.0002$), need for resuscitation at birth ($p=0.007$) and SCU admissions ($p<0.0001$). Need for ventilation did not demonstrate any between-group differences.

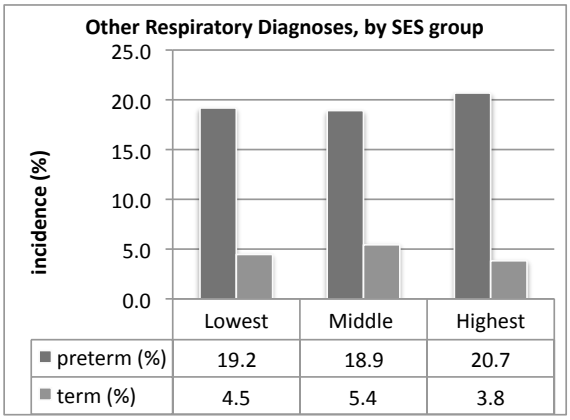
Figure 3: Percentage of infants with a diagnosis within each outcome group, by GA group and SES group.



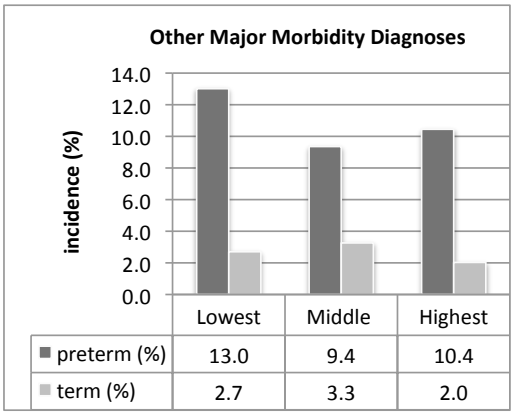
	Lowest	Middle	Highest
preterm (%)	3.3	5.4	7.25
term (%)	0.2	0.2	0.3



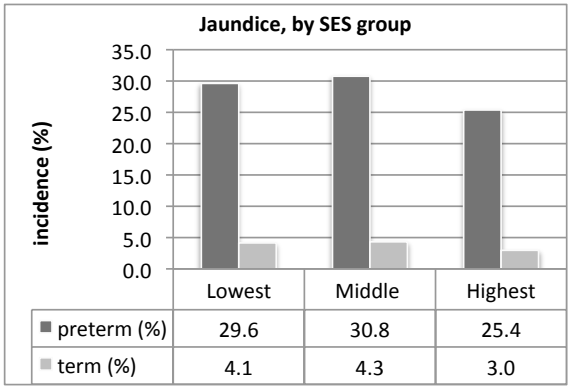
	Lowest	Middle	Highest
preterm (%)	31.0	33.3	25.4
term (%)	5.8	5.1	4.3



	Lowest	Middle	Highest
preterm (%)	19.2	18.9	20.7
term (%)	4.5	5.4	3.8

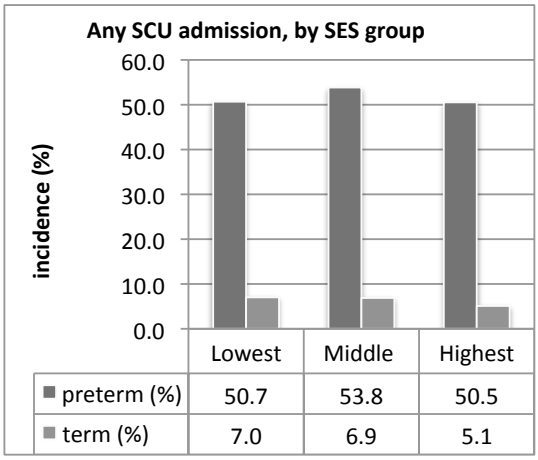


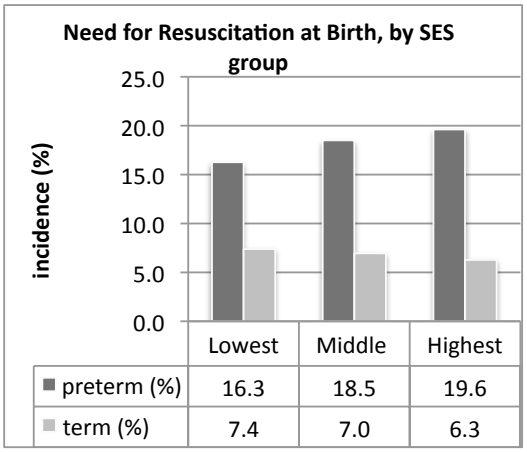
	Lowest	Middle	Highest
preterm (%)	13.0	9.4	10.4
term (%)	2.7	3.3	2.0

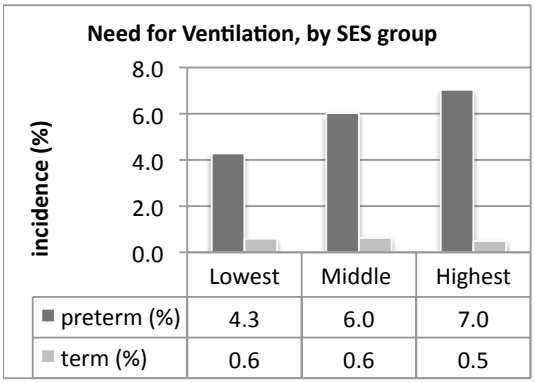


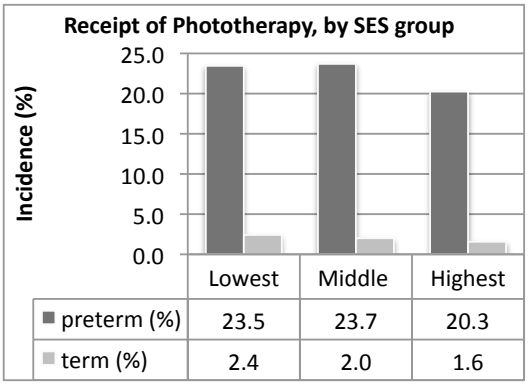
	Lowest	Middle	Highest
preterm (%)	29.6	30.8	25.4
term (%)	4.1	4.3	3.0

Figure 4: Resource utilization, by indicator, GA group and SES group









These results suggest that SES is associated with health in the immediate newborn period, which merits further investigation. The differential effect of income on term and preterm infants suggests that the planned inclusion of an interaction term of gestational age and income group is appropriate in the regression models.

Regression Analysis:

Only for the 'other major morbidity' outcome was the interaction of GA and SES significant and thus it was removed from all other models. To aid in the interpretation of results, probabilities were generated from the regression models

and are depicted in Figures 5-13. In these graphs the reference infant is from the highest income group, born to a multiparous mother in the middle age group residing in an urban centre who breastfed at discharge, born via a non-induced vaginal delivery, is a singleton female infant of appropriate size for gestational age, without diagnosed congenital anomalies and did not require resuscitation at birth.

Table 3: Regression odds ratios with 95% confidence intervals for included independent variables, for 'any diagnosis'

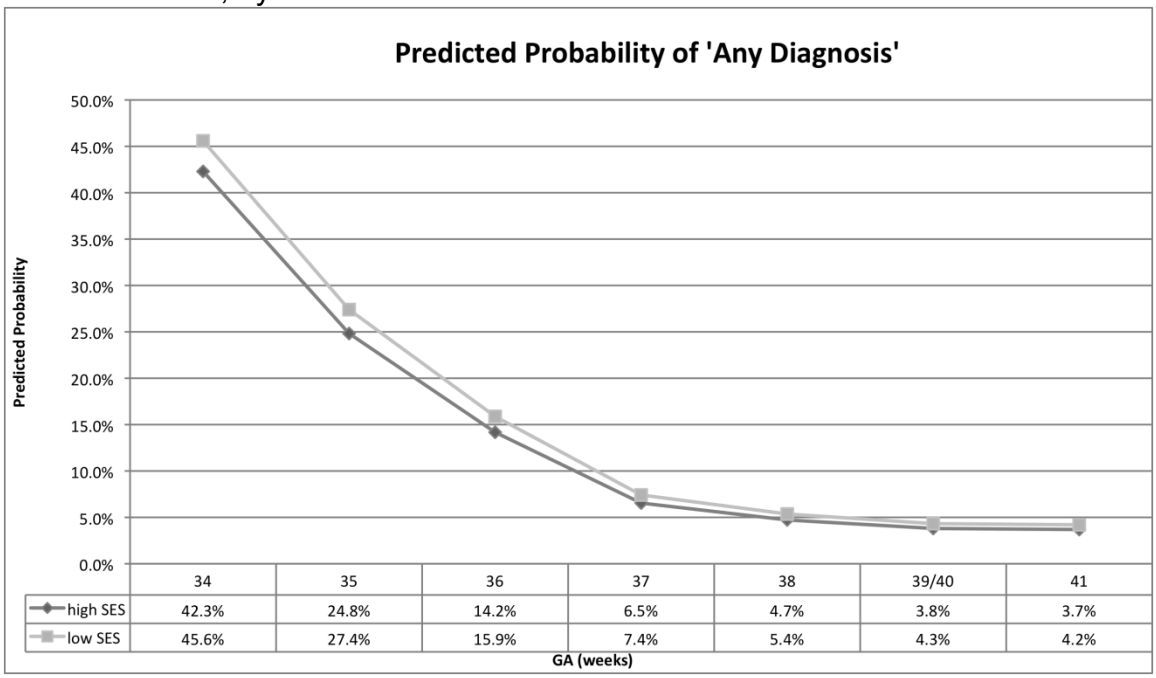
any diagnosis n=4120	OR	95% CI
maternal diabetes	**4.1**	3.5-4.7
primiparity	**1.6**	1.5-1.8
maternal age group (yrs)	p=0.10	
<19 vs 19-34	0.9	0.7-1.0
>34 vs 19-34	1.1	0.9-1.2
induced delivery	**1.4**	1.3-1.5
male infant	**1.2**	1.1-1.3
caesarean section	**1.5**	1.4-1.7
multiple gestation	0.9	0.8-1.2
SGA	**1.6**	1.4-1.8
LGA	**1.5**	1.4-1.7
any congenital anomaly	**28.8**	23.2-35.7
rural residence	1.0	0.9-1.1
any breastfeeding	1.0	0.9-1.1
need for resucitation	**3.7**	3.3-4.1
income group		
low vs middle	1.0	0.9-1.1
low vs high	**1.2**	1.1-1.4
middle vs high	**1.3**	1.2-1.4
gestational age (weeks)		
34 vs 39/40	**39.8**	27.8-57.1
35 vs 39/40	**11.1**	8.9-13.8
36 vs 39/40	**5.0**	4.3-6.0
37 vs 39/40	**1.9**	1.7-2.2
38 vs 39/40	**1.3**	1.2-1.5
41 vs 39/40	1.0	0.9-1.1

Any Diagnosis:

When overall morbidity was examined, significant associations were seen for all variables, with the exception of maternal age and multiple gestations, see

Table 3. Gestational age demonstrated a steep gradient with an OR=39.8 [27.8-57.1] at 34 weeks and persistence to 38 weeks at an OR=1.3 [1.2-1.5]. The importance of including congenital anomalies in any adjustment for newborn morbidity is demonstrated by the OR=28.8 [23.2-35.7] for this risk factor. Income demonstrated a more subtle association with infants in the lowest (OR=1.2 [1.1-1.4]) or middle (OR=1.3 [1.2-1.4]) income group more likely to receive a diagnosis compared to the highest income group. Maternal diabetes increased the odds of any diagnosis by greater than 4.5 times, even when size for gestational age was controlled for. The small but persistent effect of SES is demonstrated in Figure 5, with the predicted probability of any diagnosis remaining significantly lower in infants from higher SES groups at all points. Due to the low absolute risk the lines seem to converge. The relative increase increases as GA increases, from 10.5% at 35 weeks, to 13-14% at 37 weeks and above.

Figure 5: Predicted probability of 'any diagnosis' during birth hospitalisation, for reference infant, by GA and SES



	34	35	36	37	38	39/40	41
high SES	42.3%	24.8%	14.2%	6.5%	4.7%	3.8%	3.7%
low SES	45.6%	27.4%	15.9%	7.4%	5.4%	4.3%	4.2%

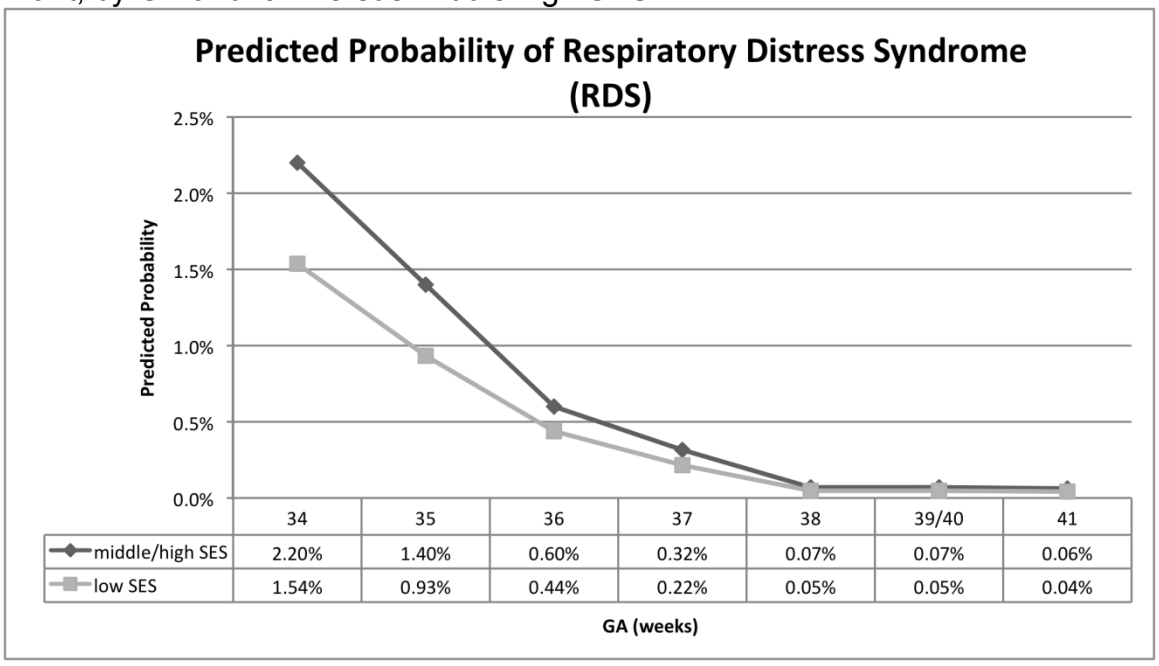
Respiratory Distress Syndrome (RDS):

The most significant predictor in this model was GA, which demonstrated an effect from 37 weeks and younger (see Table 4). The absolute predicted probability of this condition is low; for example, in the higher SES groups it was 2.2% at 34 weeks and 0.07% at 39-40 weeks, but this represents a 31-fold drop (see Figure 6). In this model the lowest income group was compared to all others to retain sample size, and was associated with a trend towards decreased odds of the condition (OR 0.7 [0.5-1.0]). Male sex, caesarean delivery, need for resuscitation at birth, presence of a congenital anomaly and decreasing gestational age increased the odds of RDS by approximately 2 to 3 times. In contrast to other models, maternal diabetes was not associated with any change in odds. Maternal age, parity, indicated delivery, multiple gestation and size for gestational age demonstrated no significant effect.

Table 4: Regression odds ratios with 95% confidence intervals for included independent variables, for prematurity related outcome groups

Prematurity Related Clinical Diagnoses	RDS n=135		Other complications of prematurity n=1167	
	OR	95% CI	**OR**	95% CI
maternal diabetes	**0.4**	0.2-1.0	**8.1**	6.9-9.5
primiparity	0.9	0.6-1.4	**1.7**	1.5-2.0
maternal age group (yrs)	p=0.86			
<19 vs 19-34	0.9	0.4-2.3	**0.7**	0.5-0.9
>34 vs 19-34	1.1	0.7-1.9	1.1	0.9-1.3
induced delivery	1.3	0.9-2.0	**1.4**	1.2-1.6
male infant	**2.0**	1.4-3.0	1.1	0.9-1.2
caesarean section	**1.9**	1.2-2.9	**1.4**	1.3-1.6
multiple gestation	1.4	0.9-2.4	1.2	0.9-1.5
SGA	0.6	0.3-1.2	**1.8**	1.5-2.2
LGA	0.9	0.5-1.6	**1.5**	1.3-1.7
any congenital anomaly	**3.0**	1.7-5.2	**2.6**	2.1-3.3
rural residence	NA		**0.8**	0.7-0.9
any breastfeeding	NA		1.0	0.8-1.1
need for resucitation	**2.0**	1.6-2.4	**1.7**	1.4-2.0
income group				
low vs middle	0.7	0.5-1.0	**1.0**	0.9-1.2
low vs high			**1.3**	1.1-1.4
middle vs high			**1.2**	1.1-1.4
gestational age (weeks)				
34 vs 39/40	**32.6**	17.8-60.0	**13.4**	10.1-17.8
35 vs 39/40	**19.6**	10.7-36.2	**8.9**	7.7-11.3
36 vs 39/40	**9.2**	4.8-17.7	**4.8**	3.9-5.9
37 vs 39/40	**4.5**	2.4-8.6	**2.1**	1.8-2.6
38 vs 39/40	1.0	0.5-2.2	**1.5**	1.3-1.8
41 vs 39/40	0.9	0.4-2.1	1.0	0.8-1.2

Figure 6: Predicted probability of 'RDS' during birth hospitalisation, for reference infant, by GA and low versus middle/high SES



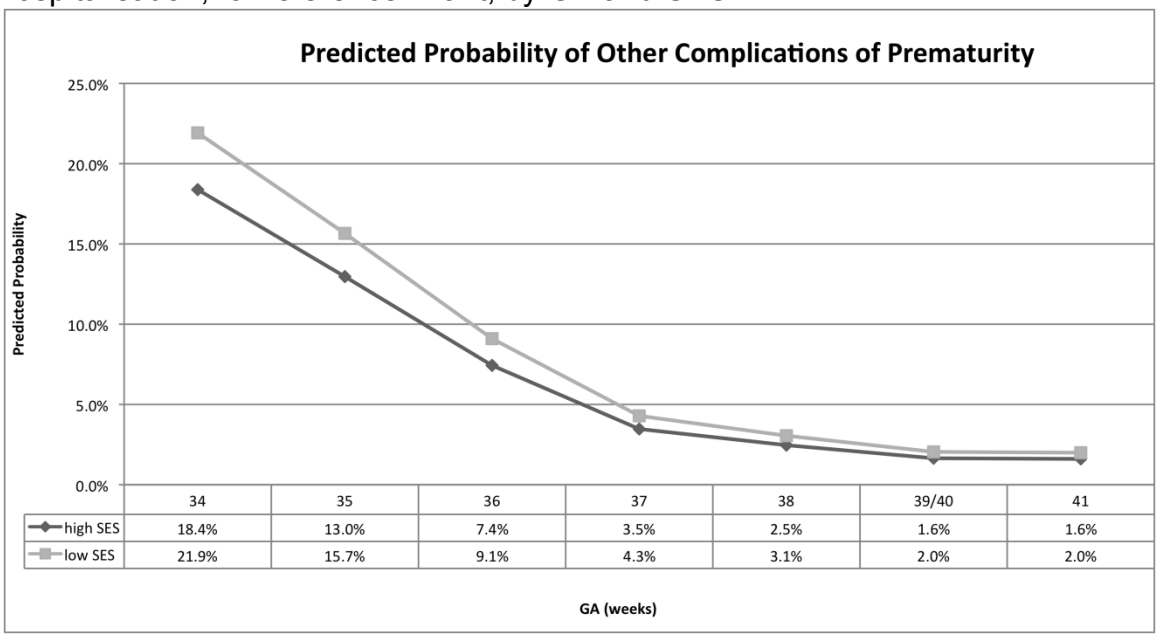
	34	35	36	37	38	39/40	41
middle/high SES	2.20%	1.40%	0.60%	0.32%	0.07%	0.07%	0.06%
low SES	1.54%	0.93%	0.44%	0.22%	0.05%	0.05%	0.04%

Other Complications of Prematurity

All risk factors demonstrated a significant association with 'other complications of prematurity' (see Table 4 and Figure 7). The effects of gestational age were significant from 38 weeks and younger, with 38 week infants having a predicted probability of 2.5-3.1% depending on income group vs. 1.6-2.0% at 39-40 weeks. This represented a 36% increased risk in the highest income group with one week change in GA. The effect of SES was small as an absolute increase but proportionally high; at each GA group the lower SES infants had a 19-24% increased predicted probability. Maternal diabetes demonstrates a strong effect again, across all income and GA groups, with an OR=8.1 [6.9-9.5]. This diagnostic group however includes hypoglycemia, which is both a complication of prematurity and maternal diabetes. Primiparity, induced or

caesarean delivery, abnormal size for gestational age, congenital anomalies and need for resuscitation at birth all increased the odds of diagnosis (see Table 4).

Figure 7: Predicted probability of 'Other complications of prematurity' during birth hospitalisation, for reference infant, by GA and SES



	34	35	36	37	38	39/40	41
high SES	18.4%	13.0%	7.4%	3.5%	2.5%	1.6%	1.6%
low SES	21.9%	15.7%	9.1%	4.3%	3.1%	2.0%	2.0%

Jaundice

For more precision, the impact of jaundice was examined using receipt of phototherapy (see section on Resource Utilization below).

Table 5: Regression odds ratios with 95% confidence interval for included independent variables, for non-prematurity related outcomes

Non-Prematurity Related Outcome Groups	respiratory (n=1392)		Other major (n=807)	
	OR	95% CI	OR	95% CI
Maternal diabetes	1.2	0.9-1.5	**1.9**	1.4-2.4
primiparity	1.2	1.0-1.3	**1.4**	1.2-1.7
maternal age group (yrs)	p=0.8561		p=0.5752	
<19 vs 19-34	0.8	0.6-1.0	1.2	0.9-1.6
>34 vs 19-34	0.9	0.8-1.1	1.0	0.8-1.2
indicated delivery	1.1	0.99-1.3	1.1	0.9-1.3
male infant	**1.4**	1.3-1.6	1.1	0.9-1.3
cesarean section	**1.8**	1.6-2.1	1.1	0.9-1.3
multiple gestation	1.0	0.7-1.3	1.0	0.7-1.5
SGA	0.8	0.7-1.1	**1.4**	1.4-2.0
LGA	1.1	0.9-1.3	**1.6**	1.4-2.0
any congenital anomaly	**2.2**	1.7-2.8	**6.4**	5.1-8.0
rural residence	**0.9**	0.8-0.99	1.0	0.9-1.7
any breastfeeding	0.9	0.8-1.0	**0.6**	0.5-0.8
need for resucitation	**6.6**	5.8-7.5	**3.8**	3.2-4.5
income group				
low vs middle	**0.9**	0.7-0.98	reported in text due to interaction	
low vs high	1.1	0.97-1.3		
middle vs high	**1.3**	1.2-1.5		
gestational age (weeks)				
34 vs 39/40	**5.8**	4.3-7.9		
35 vs 39/40	**3.5**	2.7-4.6		
36 vs 39/40	**2.9**	2.3-3.6		
37 vs 39/40	**1.3**	1.0-1.6		
38 vs 39/40	0.9	0.8-1.1		
41 vs 39/40	1.0	0.8-1.1		

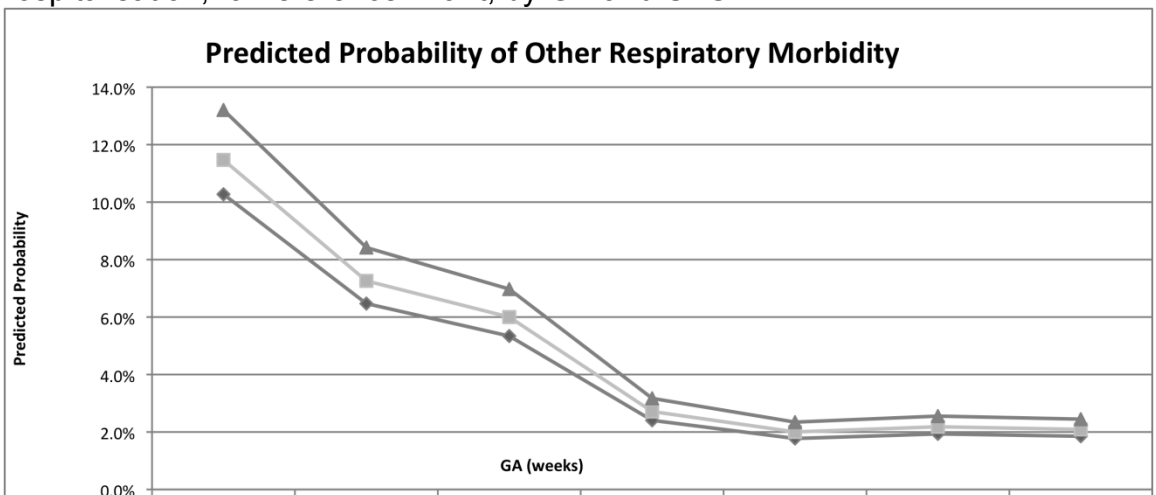
Other Respiratory Morbidity:

After controlling for the other risk factors, GA remained significant (see Table 5), falling from an OR=5.8 [4.3-7.9] at 34 weeks to an OR=1.3 [1.0-1.6] at 37 weeks after which GA was no longer significant. For SES the effect was significant in two directions depending on the comparison group. There was a decreased risk for the lowest compared to the middle group, but an increased risk from middle to highest. When the lowest and highest income groups were compared, there was no statistically significant difference. The effects of GA and

SES are most easily demonstrated in the predicted probability graph (Figure 8).

For an infant from a high SES area the probability falls from close to 10.3% at 34 weeks to 5.3% at 36 weeks and continues to fall until it levels out just under 2% (1.8-1.9%) at 38-41 weeks. The pattern is similar with a significantly increased probability for middle SES infants; these small changes in risk such as from 2.4% to 3.2% at 37 weeks translate to a high relative increase, 33% in this case. Several of the other perinatal factors demonstrated significance. Primiparity, 'induced delivery,' male sex, caesarean section delivery, and congenital anomalies were associated with increased odds of diagnosis. Being from a rural residence was associated with decreased odds. Maternal diabetes did not demonstrate a significant association (see Table 5).

Figure 8: Predicted probability of 'Other respiratory morbidity' during birth hospitalisation, for reference infant, by GA and SES

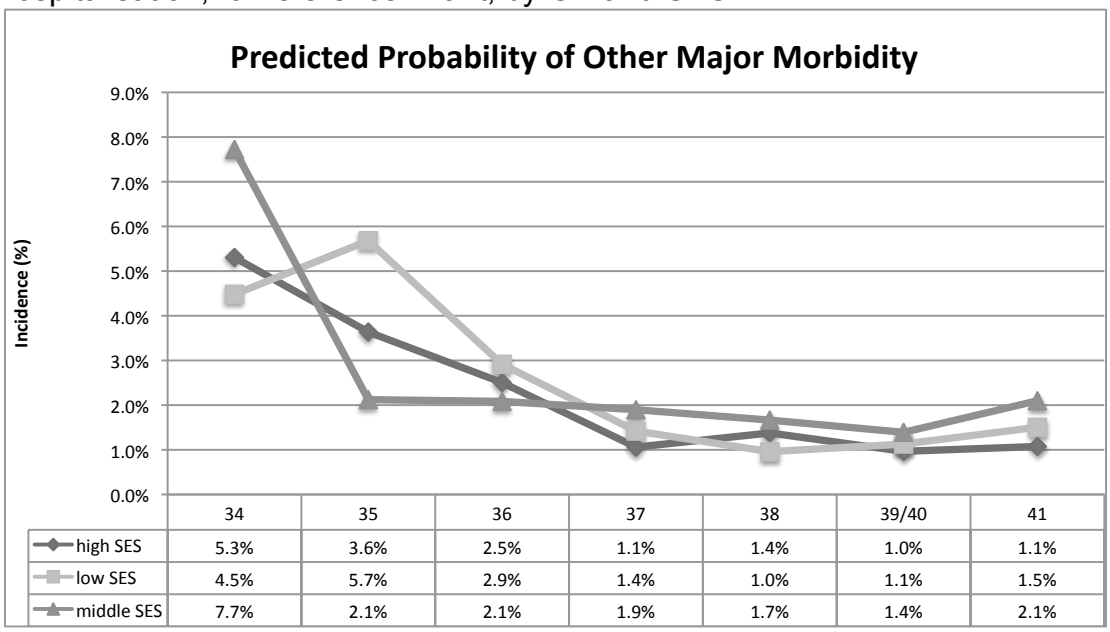


	34	35	36	37	38	39/40	41
high SES	10.3%	6.5%	5.3%	2.4%	1.8%	1.9%	1.9%
low SES	11.5%	7.3%	6.0%	2.7%	2.0%	2.2%	2.1%
middle SES	13.2%	8.4%	7.0%	3.2%	2.3%	2.6%	2.4%

Other Major Morbidity Diagnosis:

For those infants receiving other significant diagnoses, not captured in the above groups, the regression model was more complicated, as the interaction between GA and income was significant at p=0.04. The points demonstrating a significant association with SES were at 35 weeks (low vs. middle SES, OR 2.8 [1.2-6.2]), at 38 weeks (low vs. middle SES, OR 0.6 [0.4-0.9]), at 39-40 weeks (middle vs. high SES, OR 2.0 [1.2-3.2]) and at 41 weeks (middle vs. high SES, OR 1.4 [1.1-1.9]). Predicted probabilities for each week of GA and income group are shown in Figure 9. The overall trend is of decreased morbidity as GA increases, with the exception of an increase at 35 weeks for low SES infants, which may be attributed to sample size. The effect of SES, however, is variable with low SES infants faring worse overall in the preterm period, but middle SES infants faring worse at term. Maternal diabetes, primiparity, size for gestational age, congenital anomalies and need for resuscitation at birth all increased the odds of this diagnosis. Maternal age, induced delivery, caesarean section delivery, rural residence or multiple gestation did not have an association with this outcome. These infants had half the odds of being breastfed as infants without this diagnosis.

Figure 9: Predicted probability of 'Other major morbidity' during birth hospitalisation, for reference infant, by GA and SES



	34	35	36	37	38	39/40	41
high SES	5.3%	3.6%	2.5%	1.1%	1.4%	1.0%	1.1%
low SES	4.5%	5.7%	2.9%	1.4%	1.0%	1.1%	1.5%
middle SES	7.7%	2.1%	2.1%	1.9%	1.7%	1.4%	2.1%

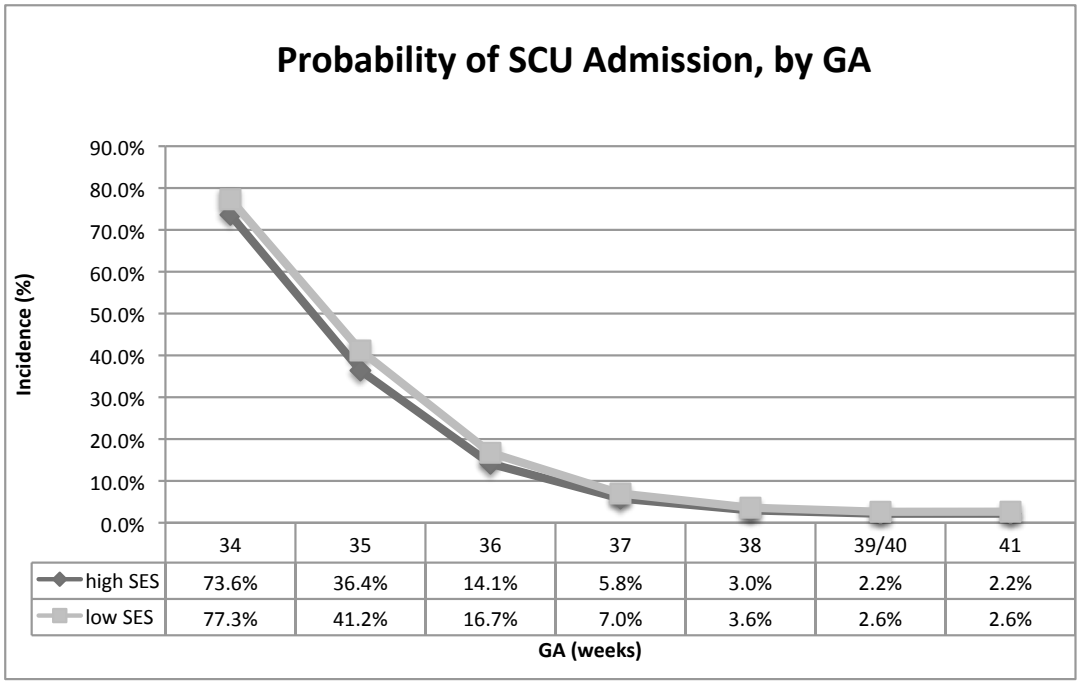
Resource Utilization:

Resource utilization was significantly associated with almost all variables, as shown in Table 6. As expected, SCU admissions fell with increasing GA, with a predicted probability of over 75% at 34 weeks and levelling off at 38+ weeks at 2.5-3% (Figure 10). Despite the very close lines on the graph, SES was significant, increasing the predicted probabilities by up to 21%, mostly at the higher GA range. Infants admitted to SCU had almost 3 times the odds of their mother being diabetic, over 4 times the odds of having received resuscitation, and over 6 times to the odds of having a congenital anomaly. The remainder of the factors had weaker, though significantly higher odds of morbidity, except for maternal age (no effect), rural residence (decreased odds), and any breastfeeding (decreased odds).

Table 6: Regression odds ratios with 95% confidence interval for included independent variables, for indicators of resource use

Resource utilization						
	SCU (n=2299)		**ventilation (n=222)**		**phototherapy (n=819)**	
	Odds Ratio (95% CI)		Odds Ratio (95% CI)		Odds Ratio (95% CI)	
maternal diabetes	**2.8**	2.4-3.4	**0.4**	0.2-0.9	**2.3**	1.8-2.9
primiparity	**1.3**	1.2-1.4	1.2	0.9-1.6	**1.9**	1.6-2.3
maternal age group (yrs)					.	
<19 vs 19-34	0.9	0.7-1.1	0.7	0.4-1.4	1.1	0.8-1.5
>34 vs 19-34	0.9	0.8-1.1	0.6	0.4-1.0	1.2	0.99-1.5
induced delivery	**1.5**	1.3-1.6	1.1	0.8-1.6	**1.3**	1.1-1.5
male infant	**1.3**	1.2-1.4	**1.4**	1.0-1.9	**1.2**	1.0-1.4
caesarean section	**1.5**	1.4-1.7	**1.9**	1.3-2.6	1.0	0.8-1.2
multiple gestation	**1.4**	1.1-1.8	0.8	0.4-1.3	**0.6**	0.4-0.8
SGA	**2.7**	2.3-3.1	1.4	0.9-2.2	**2.3**	1.8-2.9
LGA	**1.3**	1.1-1.5	0.8	0.5-1.3	**1.6**	1.3-2.0
any congenital anomaly	**6.4**	5.2-7.8	**12.9**	9.0-18.4	**1.7**	1.2-2.3
rural residence	**0.5**	0.4-0.5	**NA**		1.0	0.9-1.2
any breastfeeding	**0.7**	0.7-0.8	**NA**		**1.3**	1.0-1.6
need for resucitation	**4.6**	4.1-5.3	16.7	12.3-22.7	**1.5**	1.2-1.8
income group						
low vs middle	0.9	0.8-1.1	0.9	0.6-1.2	1.2	0.96-1.4
low vs high	**1.2**	1.1-1.4			**1.5**	1.2-1.8
middle vs high	**1.3**	1.2-1.5			**1.3**	1.0-1.5
gestational age (weeks)						
34 vs 39/40	**126.4**	85.2-187.5	**13.9**	8.4-22.8	**40.4**	29.7-55.0
35 vs 39/40	**25.9**	20.6-32.7	**7.7**	4.6-12.9	**20.2**	12.3-26.6
36 vs 39/40	**7.4**	6.2-9.0	**2.9**	1.6-5.3	**11.8**	9.2-15.1
37 vs 39/40	**2.8**	2.4-3.3	**2.8**	1.7-4.5	**3.9**	3.1-5.0
38 vs 39/40	**1.4**	1.2-1.6	1.1	0.7-1.7	**1.5**	1.2-2.0
41 vs 39/40	1.0	0.9-1.2	0.8	0.5-1.4	1.1	0.9-1.5

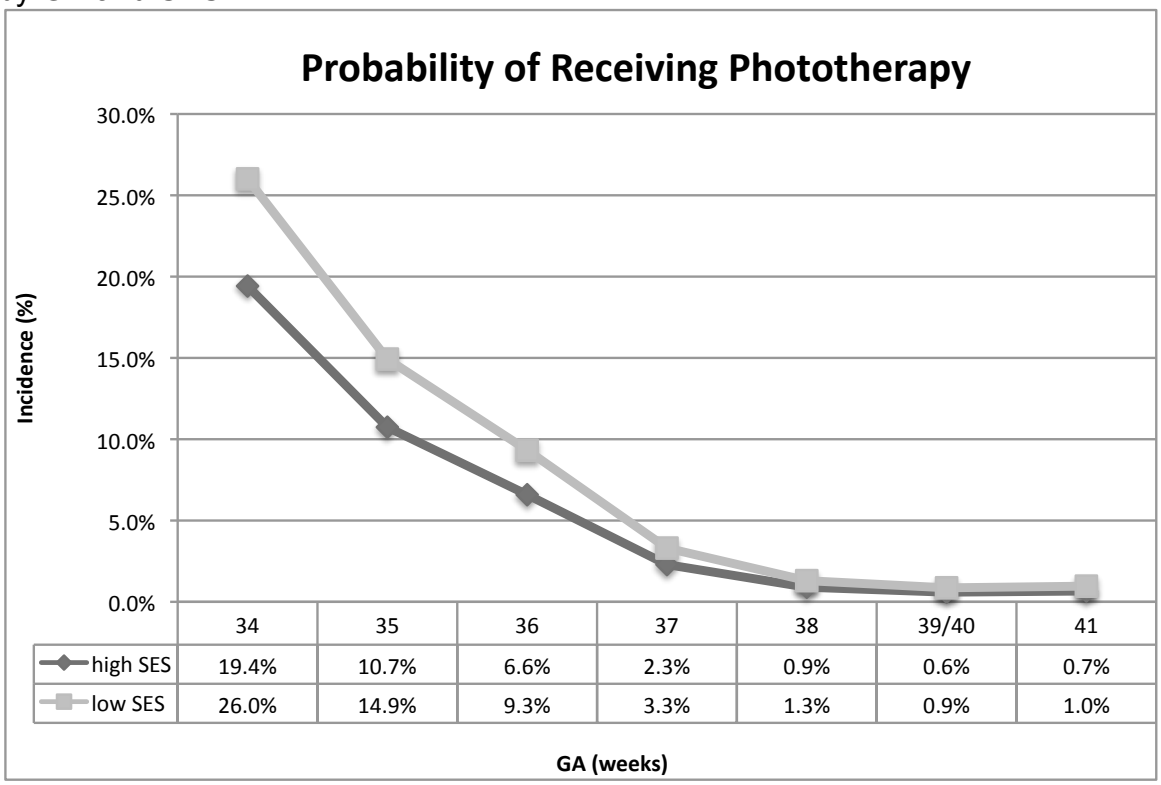
Figure 10: Predicted probability of SCU admission, for reference infants, by GA and SES



For need for ventilation, GA demonstrated the highest odds, with the effect no longer significant at 38 weeks, but significant at 36-37 weeks with odds ratios approaching 3 (see Table 6). Income did not demonstrate an effect in this model. Other variables associated with significantly increased odds were male gender, CS delivery, having received resuscitation and having a congenital anomaly. Maternal diabetes was associated with lower odds. Predicted probability was not constructed for this model.

Both income and GA were significantly associated with receipt of phototherapy (see Table 6). Even at 38 weeks, the odds of phototherapy were significantly higher than at 39 and 40 weeks. Moving from 38 to 37 weeks the predicted probability of phototherapy increased over 156%, (0.9% to 2.3%) (see Figure 11). The effect of SES was also significant, with low SES infants having 1.5 times the odds [1.2, 1.8] of phototherapy compared to high SES infants. Similar patterns are seen throughout the results. Maternal age, caesarean delivery and rural residence did not demonstrate any association. Maternal diabetes, primiparity, and being SGA were associated with approximately double the odds. Induced delivery, male gender, LGA, any congenital anomaly, breastfeeding and resuscitation at birth of the medical risk factors were associated with less than twice the odds.

Figure 11: Predicted probability of receiving phototherapy, for reference infant, by GA and SES



	34	35	36	37	38	39/40	41
high SES	19.4%	10.7%	6.6%	2.3%	0.9%	0.6%	0.7%
low SES	26.0%	14.9%	9.3%	3.3%	1.3%	0.9%	1.0%

Discussion:

This study was designed to evaluate two primary determinants of morbidity in newborn infants, GA and SES. To do so the analyses adjusted for multiple maternal and fetal variables that are disproportionately represented across these determinants. The strengths of this study include its population based sample of all preterm and term infants of 34-41 weeks GA, as compared to matched controls or a random sample from within a population, or population-based on one care provider only. It included infants cared for in many different areas including rural and urban, community and tertiary care centres, normal newborn nurseries and intensive care nurseries. The lack of individual level markers of SES was overcome using area level data, which has previously been

demonstrated as appropriate for assessing the association between SES and health outcomes.[37, 38] Very few infants were lost due to non-linkage or lack of key data. Multiple perinatal variables are controlled for within the analysis. The major weakness of the study is the inherent risk of inaccuracy of coding of disease and morbidity in administrative data. The MCHP Repository data have been utilized in the past and demonstrate good congruence with other published literature,[11,39] and the results of this study are in agreement, as discussed below.

GA demonstrated a gradient as compared to a threshold effect on morbidity. Stabilization of risk did not occur until after 37 weeks for all morbidities, the earliest at 38 weeks for respiratory morbidities, and at 39-40 weeks for non-respiratory morbidity. Resource utilization also did not plateau until 38 weeks for ventilation, and 39-40 weeks for phototherapy and SCU admission. The threshold in the 'other major morbidity' group is harder to define, as GA interacted with SES, but effects were seen throughout gestation. A consistent difference between the actual prevalence of the outcomes of interest and the predicted probability after adjustment for maternal and fetal variables was seen emphasizing the importance of the many other risk factors commonly seen in premature infants.

Short term respiratory morbidity at late preterm delivery is reported at a prevalence of 3.2-40% and at term gestations at 1-5%,[4,7,8,15,40,41] with an increase in risks extending into the 'early term' range at 37-38 weeks.[29] Quoted rates vary depending on definition and patient population and in conjunction with the rate of CS delivery.[42-44] Our RDS and 'other respiratory morbidity' incidence fall in this

range. Also confirmed in this study is the consistent association between CS delivery, male gender and respiratory morbidity. This study controlled for multiple other factors as well and demonstrated the unique effect of GA on respiratory disease after controlling for multiple other risks, demonstrating even in the 'well' preterm no stabilization of risk until 38 weeks. Percentages and risks are substantially higher in the clinical setting as the prevalence of these risk factors is high, and higher with decreasing GA. This underlines the fact that whilst the absolute risk of RDS and severe respiratory morbidity is low after 34 weeks, it is comparatively higher until 38 weeks. One study has demonstrated that increasing administration of antenatal steroids to women in labour at 34 weeks can improve mortality, with a NNT of 17.[20]

Non-respiratory complications were found at a higher prevalence than respiratory complications. Depending on patient population and which morbidities are reported, the published prevalence varies widely. Relative risks vary from around 7 to 30 at 34 weeks to 3 to 5 at 36 weeks[10, 14, 15, 20,41] for these morbidities. In this study the estimated probability after adjustment for other variables fell over five-fold from 34 weeks to 37 weeks, or alternatively if one looks from 35 to 39/40 weeks it fell by approximately half with each week of GA. These relative numbers are lower than some published risks, as this study controls for more confounders. For SCU admissions, risks vary widely as this is dependent on practice variations, especially in care of the 34 week infant but at 35-36 weeks reported RR is still greater than 10[41,44] with a prevalence as high as 30% in some studies.[45] Similar to other morbidities our predicted risk fell by

approximately half per week of GA, with a predicted risk of SCU admission at 36 weeks of 14-17% with an actual prevalence of 34%. One study calculated the number needed to harm in spontaneous singleton preterm delivery for various outcomes compared to term and found a NNH = 5.9 for NICU admission, 2.9 for a composite morbidity measure, 7.9 for respiratory morbidity, 6.5 for jaundice and 250 for CNS morbidity.[46]

Whilst it is common for studies to control for some correlates of SES such as maternal age, education and parity there are few studies which demonstrate its unique association with late preterm morbidity. This study demonstrates a small but consistent detrimental effect of low SES on morbidity after control for multiple confounders. The small changes in predicted risk would be larger in the clinical setting as the prevalence of additional risk factors is high in preterm, low SES infants. Some studies report little difference in RR after controlling for maternal age[15, 30], but associations with lack of prenatal care[15], and no effect of family income on serious neonatal morbidity.[47] This study found no unique effect of maternal age, suggesting it is the association of young maternal age with other risk factors contributing to outcomes in this patient population, notably increased preterm birth itself. Studies reporting socio-demographic characteristics frequently report the well documented association between preterm birth and low SES[11, 18, 21-26, 48-50] but not the effect of SES after birth. One recent study by Shapiro-Mendoza et al[24] reported the prevalence of composite morbidity by SES and found an effect of maternal race, insurance type, smoking, maternal age and education in term infants, and for all but maternal education in preterm infants.

They then adjusted for these factors in a regression model and found little change in the RR; they however do not report the statistics directly. Unfortunately our study was not able to control for smoking, or substance use, and possibly controlling for these factors might negate the association of morbidity with low SES seen. This suggestion of greater effects of SES on term infants was seen in our study as well, but lost after control for multiple confounders in all but the 'other major morbidity' grouping. This could be because this group represents diagnoses not casually linked to physiologic immaturity but predisposing to preterm birth, thus preserving the GA gradient.

One outcome that trended towards a protective effect of low SES was in RDS, but not clearly in the 'other respiratory morbidity' group, where there was a suggestion of an association of middle SES with higher morbidity than low SES but still the best outcome in the high SES infants. The lack of significance, and the unclear pattern could be due to the small cell sizes in each subgroup and merits further investigation. One physiologic mechanism which would be consistent with the direction of this effect involves the corticosteroid pathway. It is postulated that antenatal stress induces fetal lung maturation in growth restricted fetuses[51] and there is emerging research into how increased maternal stress worsens fetal outcomes via the stress pathway.[52] Women from lower SES groups have higher baseline stress[25,53,54] which could induce this response and may lead to fetal lung maturity at earlier gestations, similar to the effect seen in growth restricted fetuses. What is unclear in this group is the lack of an association seen between maternal diabetes and RDS, as infants born to mothers with diabetes

are reported to be at increased risk[55,56] due to delays in surfactant production. As a very high proportion of infants of diabetic mothers (IDM) are induced, 63.8% in our study, often at late preterm and early term gestation for macrosomia or poor maternal glucose control after documentation of fetal lung maturity via amniocentesis, this could be reflected in lower respiratory morbidity. As IDM are frequently born in low SES situations there may be an interaction between the two effects not explored in the model. The effect of maternal diabetes, both gestational and pre-gestational, merits further investigation in this dataset, as there is a high prevalence of maternal diabetes and the ability to incorporate physician-billing data pre-pregnancy to properly classify exposure.

It is both the gradient of morbidity and the absolute risks that merit attention in the late preterm, and even in the term infant. The absolute risks are low but proportionally higher than term infants, and due to their large numbers they utilize more resources than the more preterm infant.[6,27,28] Low percentage rates transmit to high numbers; for example 243, 273 and 352 infants admitted to NICU, or 114, 197 and 324 infants with 'other complications of prematurity' at 34, 37 and 38 weeks respectively. The consistent demonstration of increased need for resuscitation in this and other studies[4,7,8,57] underlines the importance of having skilled practitioners at these deliveries as timely management of perinatal depression improves outcome and can often avert the need for NICU admission. The persistence of elevated relative risks up to 37 and sometimes 38 weeks GA underlines the importance of per week analysis; changes in the composition of 'term' controls can impact the validity of studies.

While the severity of these morbidities is often not high they lead to increased resource use and medical interventions. Any medical intervention brings with it risks to the patient, especially from interventions like gavage feeding and intravenous administration of fluids and medications. Admission to an SCU or medical interventions to the infant can cause significant parental anxiety, and separation of mother-infant pairs can have long lasting effects[58] especially in regard to initiation of breastfeeding, which is already at risk due to late preterm birth.[59] The persistence of these risks into early term gestation underlines the importance of risk versus benefit considerations when elective or semi-elective delivery is planned. The estimation of risk due to prematurity must include not only respiratory but other morbidities as well and account for the differences in physiologic maturity at any GA. Lastly parents need to be educated before and following the birth of late preterm or early term infants so as to know what to expect and how to best care for their infants.

The effect of GA remained strong and consistent even after the influence of multiple other maternal and neonatal complications were removed. Fetal maturity as a gradient has been clearly demonstrated over multiple diagnostic groups, with and without infants with congenital anomalies. Stabilization of risk does not occur at 37 weeks, the definition of term gestation, but between 37 and 40 weeks depending on the outcome of interest. The effect of SES was small but significant after controlling for other confounding influences. This suggests that the effect of SES may be mediated primarily, but not completely, through its effect on increasing maternal and fetal complications. This suggests that timely

interventions to preserve the relatively good health of low SES infants at birth could be beneficial in improving long-term outcome. This stands in contrast to the later neonatal and childhood periods where SES is known to exert a much greater effect on morbidity. Due to the large and increasing number of late preterm infants, strategies to reduce inappropriate late preterm delivery and improve care for these infants once delivered will have large public health impacts. These plans must address both the socioeconomic determinants of preterm birth as well as its impact on the infant to improve long-term outcomes.

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Chapter 5: Neonatal Readmissions

Preterm birth rates are increasing, and a disproportionate amount of that increase is accounted for by the late preterm infant,[1,2] those born at 34 to 36 weeks of gestational age (GA). Following some early studies demonstrating increased neonatal complications[3,4] there has been increasing research into this area, predominantly focusing on in-hospital morbidity in the early neonatal period[4-9] and with little focus on the impact of socioeconomic status (SES) which is associated with higher rates of prematurity and overall morbidity.[1,10-16]

There is an abundance of literature on neonatal readmission risk, primarily following the change to shorter postpartum stays, though little specific to late preterm infants. Studies including preterm infants frequently examine all preterm infants together,[12] concentrate on respiratory readmissions only,[17-19] or are studies of 'term' infants which include the late preterm infant. This is most common when studies look at readmissions for jaundice.[20-24] There is little on the late preterm infant exclusively or the influence of SES on the outcomes for these infants.[12,25-30]

One Manitoba study found that both SES and prematurity were independently related to readmission rates. It examined both preterm delivery and multiple markers of low SES including young maternal age, low area-level income and area of residence.[12] The current study will expand that further, looking specifically at late preterm birth and SES together as risk factors for readmission. There are many reasons to postulate that lower SES late preterm infants will be less healthy and experience more complications than higher SES

preterm infants. We know that SES impacts uptake of prenatal care[31], nutritional and growth status of the fetus[32] and frequently results in low or very high birth weight. Lower SES mothers are more likely to have poorly controlled gestational diabetes, use illicit substances and alcohol during pregnancy, smoke cigarettes or experience physical abuse.[33] In the perinatal period low SES mothers are less likely to have social support, less likely to have a stable living environment and food security, less likely to breastfeed and more likely to experience postpartum depression and higher levels of both measured and perceived stress.[13, 34, 35] The impact of these factors on the health status of, and care required for, a late preterm infant is unknown and this study examined the impact of these factors on neonatal hospital readmission.

Methods:

A retrospective cohort study was undertaken utilizing data housed at the Manitoba Centre for Health Policy (MCHP). The Population Health Research Data Repository (Repository) at the MCHP contains a number of anonymized administrative datasets maintained by Manitoba Health. This study utilized data from hospital discharge abstracts, Vital Statistics, and population registry data as well as public access Canada Census files and data from Family Services. The results and conclusions are those of the authors and no official endorsement by the providers of the data is intended or should be inferred. The Repository contains information on almost all residents of Manitoba, with the exception of RCMP officers, inmates of federal penitentiaries and members of the Canadian Armed Forces. Appropriate approvals were obtained from the custodians of all

information sources in addition to the University of Manitoba Health Research Ethics Board and the Health Information Privacy Committee of Manitoba.

The study population included all infants born at 34 – 41 completed weeks gestation during the fiscal years 2004/2005 to 2005/2006, who remained in Manitoba until their first birthday. It also includes the linked maternal file for extraction of pregnancy related variables. The initial dataset contained 25 834 newborn records that were matched with population registry (22 unmatched) and maternal health records (2 unmatched) successfully for 25 810 infants. Of these, 436 moved before their first birthday and 62 were missing essential demographic data (birth weight, GA or income data) and were removed from the analysis, thus resulting in a final cohort of 25 312 infants. Income and gestational age distribution of those infants who moved did not differ significantly from those retained in the sample (see Chapter 2). There were 3 993 discrete hospitalisations, after inter-hospital transfers were merged into one admission. Infants classified as boarder infants, that is, those infants admitted to accompany another requiring care, usually their mother, not due to their own illness, were not included in the analysis, they constituted 323 of the admission episodes, leaving a total of 3 670 admission episodes in infants up to 365 days of age. Counts of admissions were generated from these records and merged to the mother-infant pair records.

Two different variables were used to assign infants to an SES group using maternal data. An individual level variable, receipt of provincial income assistance by the mother in the month of delivery, placed an infant in the lowest SES group. Area-level income information on average household income from

Canada Census data was aggregated at the dissemination area level (approximately 400 persons) and grouped into population quintiles. Income quintiles were used to place the infants not on income assistance into one of the three groups. Infants in income quintile 1 were placed in the lowest group along with the income assistance recipients; quintiles 2 and 3 were placed in the middle group, and quintiles 4 and 5 in the highest group. GA was taken from the hospital record, which was based on menstrual dates or ultrasound dating unless the clinical estimate at delivery differed in the opinion of the physician of record.

Maternal Variables:

Maternal codes taken from the hospital record included maternal age (years) and parity. The presence of maternal diabetes was established using maternal ICD10 codes[36] from the hospital abstract. There was no distinction made between types of diabetes, as insufficient clinical data on the maternal history is available from the database. Rural location is defined by postal codes outside of Winnipeg or Brandon on the maternal record. Receipt of income assistance was taken from the Manitoba Family Services and Consumer Affairs, Employment and Income Assistance database.

Newborn Variables:

Infant gender, birth date, birth weight, breastfeeding at initial birth discharge, and length of initial birth stay are taken from the newborn record. Some composite variables reflecting newborn complications, include birth morbidity, need for ventilation, or special care unit (SCU) admission are retained from an earlier study of birth hospitalisation outcomes. Birth morbidity includes

both major and minor complications experienced during the birth hospitalisation, and separates the 'well' infant from the 'unwell' infant, even for relatively minor issues. Need for ventilation was to control for those infants who required a high level of care at birth and may have residual effects. SCU admission was chosen as in some studies it exerted a protective effect for readmissions.[25] Further details of these variables can be found in Chapter 4 and Appendix 1. Infants are classified as having a congenital anomaly (CA) if they received a diagnostic code at any time during that year from the significant congenital anomalies group (see Appendix 1).

Outcomes:

Neonatal readmissions were defined as those occurring up to 28 days of age. Overall admissions at up to 28 days after discharge, as this is an alternative used in the literature, will also be reported; subgroup analysis of neonatal readmissions occurred for those up to 28 days of age only. This was chosen to reflect the influence of the 'well' term and preterm infant more than those with a protracted stay. The 'most responsible diagnosis' from the first episode in the encounter was assigned as the reason for admission. Unless otherwise indicated, all results are for any admission within the category, infants with multiple admissions within the same category are only represented once.

For neonatal readmissions, six diagnostic groupings were created:

1. **Respiratory:** both infectious and non-infectious causes of respiratory illness, including apnea and apparent life threatening events (ALTE).

2. Jaundice: all types of jaundice including conjugated and unconjugated hyperbilirubinemia. This includes but is not limited to 'normal newborn' or physiologic jaundice, breastfeeding jaundice, inborn errors that present as jaundice and hemolytic disease causing jaundice.

3. **Infection**: includes all non-respiratory infections, viral or bacterial, including but not limited to septicemia, urinary tract infections/urosepsis, gastro-intestinal infections, cellulitis and meningitis. It includes those infants admitted with fever to rule out sepsis.

4. **Feeding**: includes those infants admitted for feeding difficulty, excessive weight loss or failure to thrive.

5. **Congenital Anomaly**: includes those infants for whom the most responsible diagnosis was a 'significant congenital anomaly' code specified previously (Appendix 1).

6. **All other**: includes all infants for whom the 'most responsible diagnosis' code is not found in one of the above groups.

Please see Appendix 1 for specific ICD10 codes utilized.

Regression models were constructed to control for the effect of other perinatal variables. GA was entered as a classed variable with 40 weeks as the reference. Maternal age was entered as a categorical variable with three groups (<19, 19-34 and >35 years). The 19-34 year age group was used as the reference. Socioeconomic status was analyzed using the income groups

previously described, with highest SES as the reference. The remainder of the variables were binomial. Logistic regression models with admission as a binomial outcome were initially run with an interaction variable for SES and GA, but the interaction was dropped in all models because it was not significant. Due to the possible differential effect of a short birth stay (2 days of less) depending on gestational age it was entered as an interaction with GA, and retained if significant. A two day length of stay was chosen as this was the median length of stay for term infants, under the assumption that preterm infants discharged after this length of stay are being treated as term. Significance was set at $p<0.05$. All data handling and statistical analysis was done using SAS software, Version 9.1 for Unix.[37] For probability comparisons, a reference infant was defined as born to multiparous mother without diabetes, from the 19-34 year age group. The reference infant was female, breastfed, without congenital anomalies, living in an urban setting and did not experience birth morbidity, SCU admission or ventilation.

Results:

For characteristics of the study cohort by GA at birth and SES group please see Tables 1-2. Of the 25 312 infants in the birth cohort, 6.1% (n=1524) were born preterm at 34 to 36 weeks GA.

Table 1: Characteristics of study population by GA at birth and selected maternal and neonatal variables

GA	34	35	36	37	38	39	40	41
n	276	457	801	1780	4189	6535	7218	4056
Maternal Characteristics								
maternal age group, years								
<19	5.8	3.5	4.2	4.9	4.4	5.4	5.1	5.5
19-34	80.4	81.2	78.0	79.0	80.5	82.2	83.5	83.3
>34	13.8	15.3	17.7	16.1	15.1	12.4	11.4	11.2
primiparous, %	44.2	39.6	36.6	35.7	32.5	35.1	39.4	46.8
CS, %	35.9	33.7	29.0	24.9	30.1	21.2	13.9	17.2
induced delivery	26.8	35.2	35.0	33.7	34.8	22.1	16.4	39.1
multiple birth	23.6	21.9	11.7	8.0	2.7	0.3	0.2	0.0
maternal diabetes	7.6	12.0	17.2	10.1	8.5	3.8	2.4	0.8
low SES	35.9	37.2	39.3	36.8	33.6	31.8	31.2	30.4
Newborn Characteristics								
male, %	58.0	55.4	54.2	51.7	53.0	49.6	50.1	51.9
mean BW, grams (SD)	2377 (460)	2640 (534)	2936 (530)	3143 (480)	3358 (479)	3496 (459)	3656 (463)	3774 (469)
BW range	1184-3902	1216-4599	1420-5160	1172-5305	1610-6440	1703-6457	1349-5589	1438-5795
median LOS (range)	13 (1-90)	6 (1-66)	3 (1-71)	2 (1-103)	2 (1-168)	2 (1-93)	2 (1-55)	2 (1-42)
any neonatal morbidity, %	85.5	62.4	45.3	23.4	17.6	11.6	11.6	12.1
major congenital anomaly, %	10.1	5.7	5.6	3.2	3.1	2.1	1.7	2.1
short stay, %	7.3	11.8	28.2	56.7	61.3	70.9	74.9	70.6

Please see text for description of variables, CS=cesarean section, SES=socioeconomic status, BW=birthweight, LOS=length of stay

Table 2: Characteristics of study population by SES and selected maternal and newborn characteristics

SES group	lowest	middle	highest	chi-sq
n	8203	8854	8255	
Maternal Characteristics				
maternal age group, yrs <19	10.3	3.3	1.7	p<0.0001
19-34	81.6	83.7	80.8	p<0.0001
>34	8.1	12.9	17.5	p<0.0001
primiparous, %	33.3	40.2	40.6	p<0.0001
CS, %	17.5	21.9	23.0	p<0.0001
maternal diabetes	7.2	4.2	3.0	p<0.0001
induced delivery	25.5	27.9	26.9	p=0.0014
multiple birth	1.7	2.0	2.8	p<0.0001
rural	45.8	44.5	42.3	p<0.0001
Newborn Characteristics				
male, %	51.3	51.4	51.0	p=0.7066
mean BW, grams (SD)	3482 (554)	3505 (534)	3492 (526)	
BW range	1216-6208	1172-6457	1331-5746	
median LOS (range)	2 (1-103)	2 (1-168)	2 (1-51)	
premature	7.1	5.4	5.7	p=0.0001
any neonatal morbidity, %	17.7	17.2	14.0	p<0.0001
major congenital anomaly, %	2.8	2.6	2.1	p=0.0046
short stay, %	67.0	65.3	66.6	p=0.0559

BW=birthweight, CS=cesarean section, LOS=length of stay, SES=socioeconomic status

In the cohort 3.4% (n=860) of all infants experienced at least one readmission at up to 28 days of age, with preterm infants accounting for 11.6% (n=100) of these. Despite making up 32.4% of the cohort, 38.6% (n=332) of readmissions were infants from the lowest SES group. For up to 28 days post discharge, an admission frequency of 4.4% (n=1125) was found. Number and percentage of infants by GA and reason for admission is shown in Table 3. Infants may be in more than one category if the experienced more than one admission, where the second was from a different category. There were 37 infants with 2 admissions during the first 28 days of life.

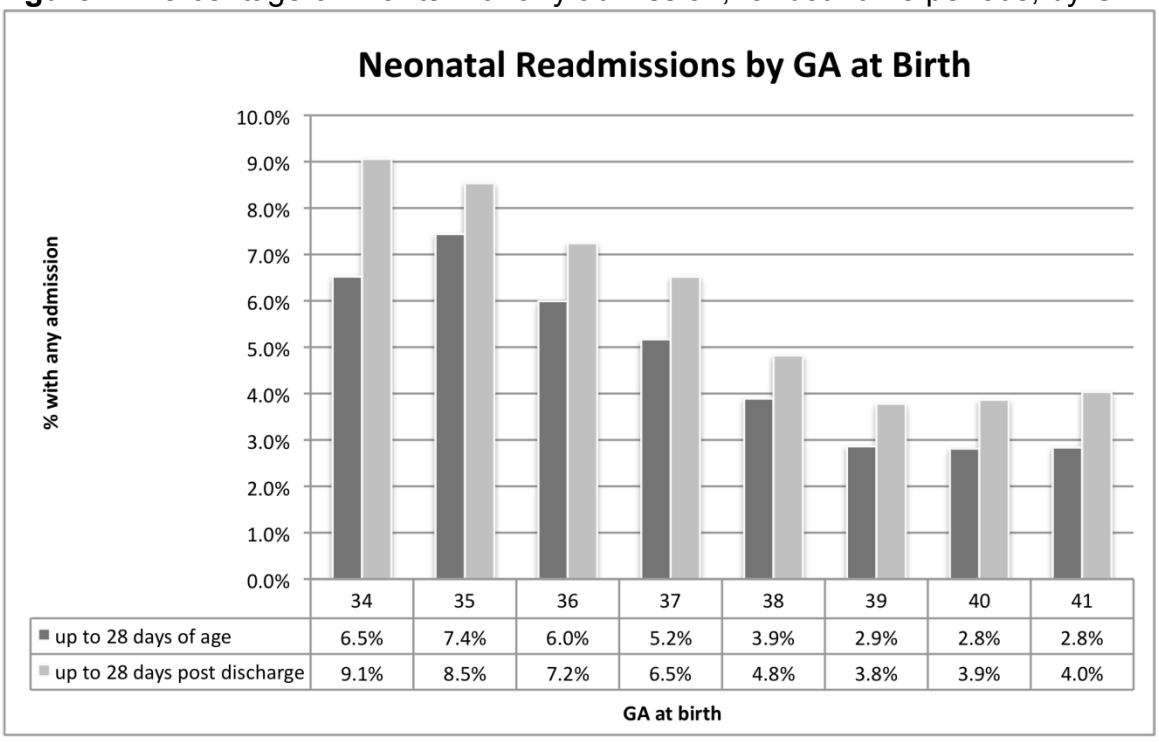
Table 3: Number and percentage of infants with at least one admission at up to 28 days of age, by reason for admission and GA group

reason for admission	respiratory	jaundice	infectious	feeding	congenital anomaly	other
total # number admitted	171	173	126	68	88	255
preterm	23	22	supressed	10	7	33
% of infants	0.7%	0.7%	0.5%	0.3%	0.3%	1.0%
% of admitted infants	19.9%	20.1%	14.7%	7.9%	10.2%	29.7%

infants may be represented in more than one admission group, thus totals exceed 100%

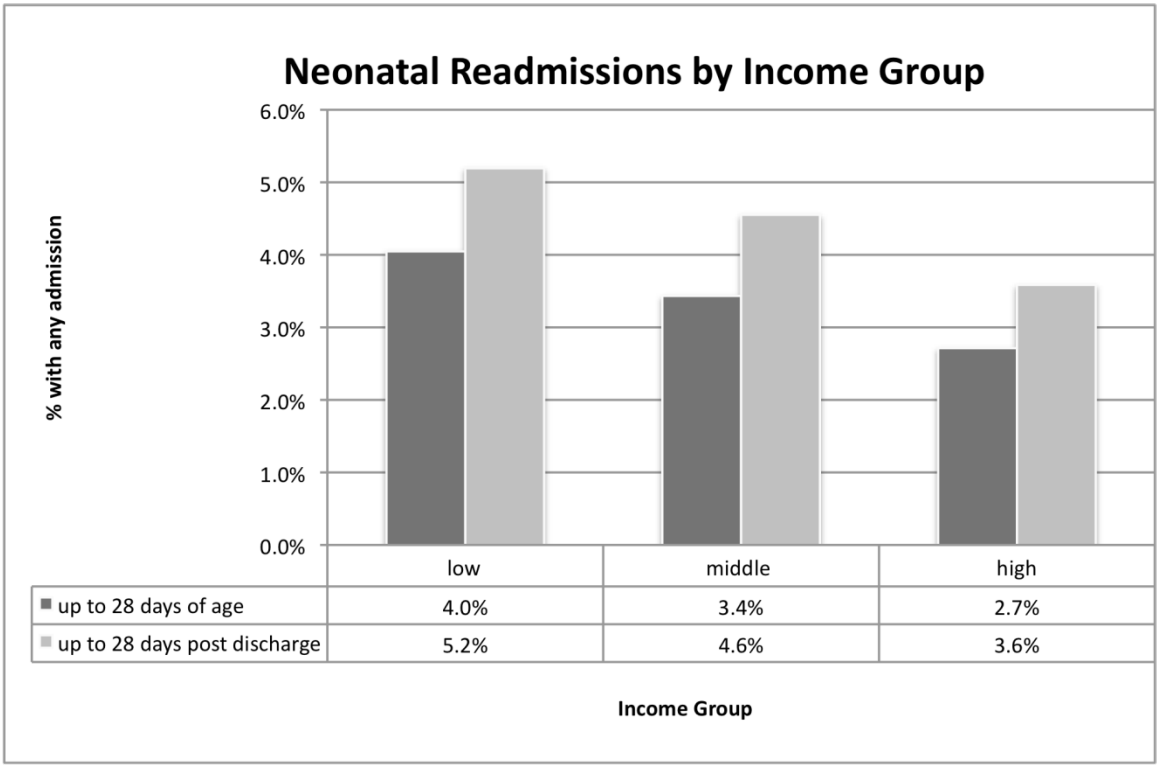
Percentages of infants experiencing any admission by GA or SES are shown in Figures 1-2. There was a decrease in readmissions as GA increased, with a plateau at 39 weeks. There was a decrease in readmissions as SES increased, a fall by approximately a third from lowest to highest income group. When admissions at up to 28 days of age were examined a higher incidence of admissions in the 35 (7.4%) compared to the 34 (6.5%) week GA infants was seen, otherwise the pattern was similar to that of the 28 days post discharge infants, for both GA and SES.

Figure 1: Percentage of infants with any admission, for both time periods, by GA



	34	35	36	37	38	39	40	41
up to 28 days of age	6.5%	7.4%	6.0%	5.2%	3.9%	2.9%	2.8%	2.8%
up to 28 days post discharge	9.1%	8.5%	7.2%	6.5%	4.8%	3.8%	3.9%	4.0%

Figure 2: Percentage of infants with any admission, for both time periods, by SES



	low	middle	high
up to 28 days of age	4.0%	3.4%	2.7%
up to 28 days post discharge	5.2%	4.6%	3.6%

Regression models were constructed to control for various maternal and neonatal characteristics disproportionately represented across the GA and SES strata (see Tables 1-2). There were no interactions between GA and SES, so the interaction term was dropped from the models. This allowed for usage of another interaction term, short stay at birth and GA at birth. This interaction was significant in the 'any admission' model for both admissions up to 28 days of age and 28 days after discharge, as well as for respiratory admissions. It was dropped from the other models as it was not significant. Two thirds of infants in this cohort, 66.3% were short stay infants. For ease of comparison, graphs of the predicted probability of admission by GA and SES for a reference infant are shown in those outcomes where the interaction was significant.

Regression Models:

Any readmission:

Patterns were similar whether neonatal readmissions were classified using the up to 28 days after birth (Table 4, column 1) or after discharge (Table 5) definition. All further analyses within this admission group or others are for admissions at up to 28 days of age only. The interaction between GA and short stay was significant, with short stay associated with a greater increase in odds of admission at lower gestations (Table 4). There was an over six-fold fall in odds from 34 to 38 weeks in short stay infants. There was a slight increase in probability of admission at 37 compared to 36 weeks. Those infants who stayed longer than 2 days showed no significant effect of GA. The effect of SES is seen in an absolute increase of 2% in admissions. This translates to a 30% increased

predicted probability of readmission for a low SES infant compared to a high SES infant. The importance of controlling for confounders is demonstrated by the significant increase in odds seen in infants born to primiparous mothers, male infants, those infants who experienced a neonatal morbidity, had a congenital anomaly or needed ventilation in the immediate newborn period and for those infants in a rural community. Maternal age and diabetes did not change the odds of admission. An SCU admission at birth came very close to reducing the odds of neonatal readmission, OR=0.8 [0.6-1.0]. Please see Table 4 for specifics.

Table 4: Regression odds ratios with 95% confidence intervals, models with significant interactions, by reason for admission at up to 28 days of age

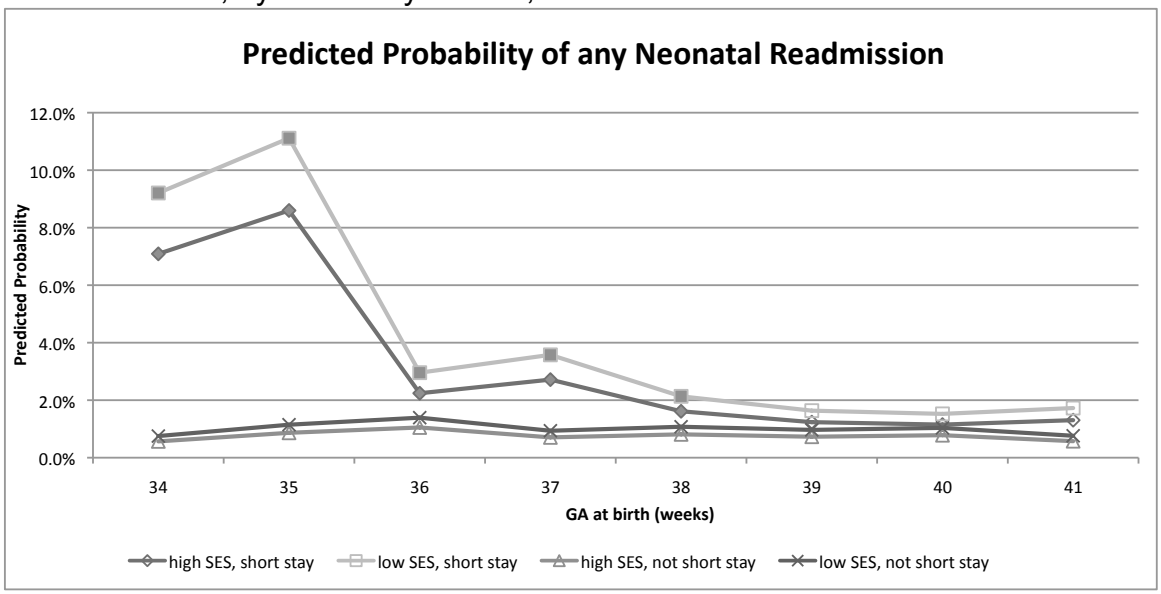
Variable	any neonatal readmission, n=859		respiratory, n=171	
	OR	**95% CI**	**OR**	**95% CI**
maternal diabetes	1.2	0.9-1.6	0.8	0.4-1.5
primiparity	**1.2**	1.0-1.4	0.8	0.6-1.2
maternal age group	p=0.30		p=0.14	
<19 vs 19-34	1.1	0.8-1.5	1.3	0.7-2.4
>34 vs 19-34	1.2	0.9-	0.6	0.3-1.1
ventilation	**1.8**	1.1-2.8	**5.5**	2.6-12.0
male sex	**1.4**	1.2-1.6	1.2	0.9-1.7
birth morbidity	**3.3**	2.7-4.0	**7.9**	5.5-11.4
any SCU stay	0.8	0.6-1.0	**0.5**	0.3-0.9
congenital anomaly	**4.7**	3.7-5.9	**0.4**	0.2-0.8
rural residence	**1.5**	1.3-1.8	**1.9**	1.3-2.6
jaundice				
any breastfeeding	0.9	0.7-1.0	**0.6**	0.4-0.8
income group			p=0.24	
low vs middle	1.1	0.9-1.3	1.4	0.9-2.0
low vs high	**1.3**	1.1-1.6	1.2	0.8-1.9
middle vs high	**1.2**	1.0-1.4	0.9	0.6-1.4
Effect of short stay vs. not short stay at:				
Gestational Age (weeks) 34	**13.4**	3.8-47.2	**28.4**	4.2-191.1
35	**10.8**	4.7-25.0	**13.1**	1.9-89.4
36	**2.2**	1.1-4.2	**5.1**	1.5-17.7
37	**3.9**	2.4-6.4	**14.4**	1.8-114.6
38	**2.0**	1.4-2.8	**3.4**	1.4-8.1
39	**1.7**	1.2-2.4	**2.1**	1.0-4.3
40	**1.5**	1.1-2.1	1.5	0.7-3.1
41	**2.3**	1.3-3.6	**3.9**	1.3-11.6
Effect of GA (weeks) in short stay, vs. 40 weeks				
34	**6.6**	2.2-19.3	**10.8**	7.0-38.3
35	**8.1**	4.0-16.2	**3.7**	2.6-14.3
36	**2.0**	1.1-3.5	**3.4**	1.6-8.6
37	**2.4**	1.8-3.3	1.6	0.6-3.4
38	**1.4**	1.1-1.8	1.6	0.5-2.8
39	1.1	0.8-1.4	1.2	0.3-2.1
40	REF		REF	
41	1.1	0.9-1.5	1.5	0.4-2.7

significant OR in bold, REF=reference group

Table 5: Regression odds ratios with 95% confidence intervals, for any admission at up to 28 days post discharge from birth hospitalisation

Variable	<= 28 days post discharge, n=1124	
	OR	95% CI
maternal diabetes	1.2	0.9-1.5
primiparity	**1.2**	1.1-1.4
maternal age group	p=0.31	
<19 vs 19-34	1.2	0.9-1.5
>34 vs 19-34	1.1	0.9-1.3
ventilation	**1.7**	1.2-2.6
male sex	**1.4**	1.2-1.5
birth morbidity	**2.6**	2.1-3.0
any SCU stay	0.9	0.7-1.2
congenital anomaly	**4.3**	3.5-5.4
rural residence	**1.5**	1.3-1.7
jaundice		
any breastfeeding	1.0	0.9-1.2
income group		
low vs middle	**1.1**	1.0-1.3
low vs high	**1.4**	1.2-1.6
middle vs high	**1.2**	1.1-1.4
Interaction of short stay and GA	p<0.0001	

Figure 3: Predicted probability of any readmission at up to 28 days of age, for reference infant, by short stay at birth, GA and SES

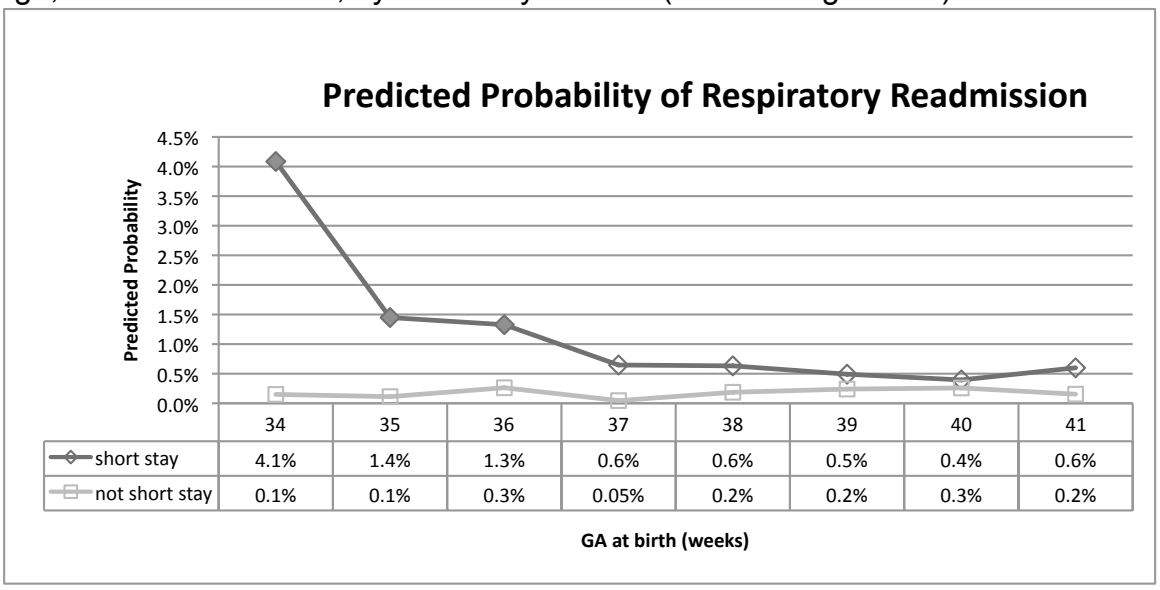


Points where GA is significant vs. 40 weeks are filled, non-significant are open
SES and short stay were significant at all GA points

Respiratory:

The interaction of GA and short stay was significant for respiratory admissions, (See Table 4, column 2) again with higher odds in 34 to 35 week infants, a drop at 36 weeks and an increase again at 37 weeks. Short stay was significant at all gestations, and for these infants there was a dramatic decrease from 34 to 35 weeks, a plateau at 35-36 weeks, and a fall of over two thirds by 40 weeks in predicted admissions (see Figure 4). Infants staying greater than two days had no significant effect of GA. SES did not demonstrate a significant effect in this model. An SCU stay, having a congenital anomaly, birth morbidity and any breastfeeding reduced the odds of readmission, but ventilation in the newborn period did not. In comparison to other outcomes male sex was not associated with increased odds of readmission. Short stay was significant at all GA points except 40 weeks.

Figure 4: Predicted probability of any respiratory readmission at up to 28 days of age, for reference infant, by short stay and GA (SES not significant)



Points where GA is significant vs. 40 weeks are filled, non-significant are open

Jaundice:

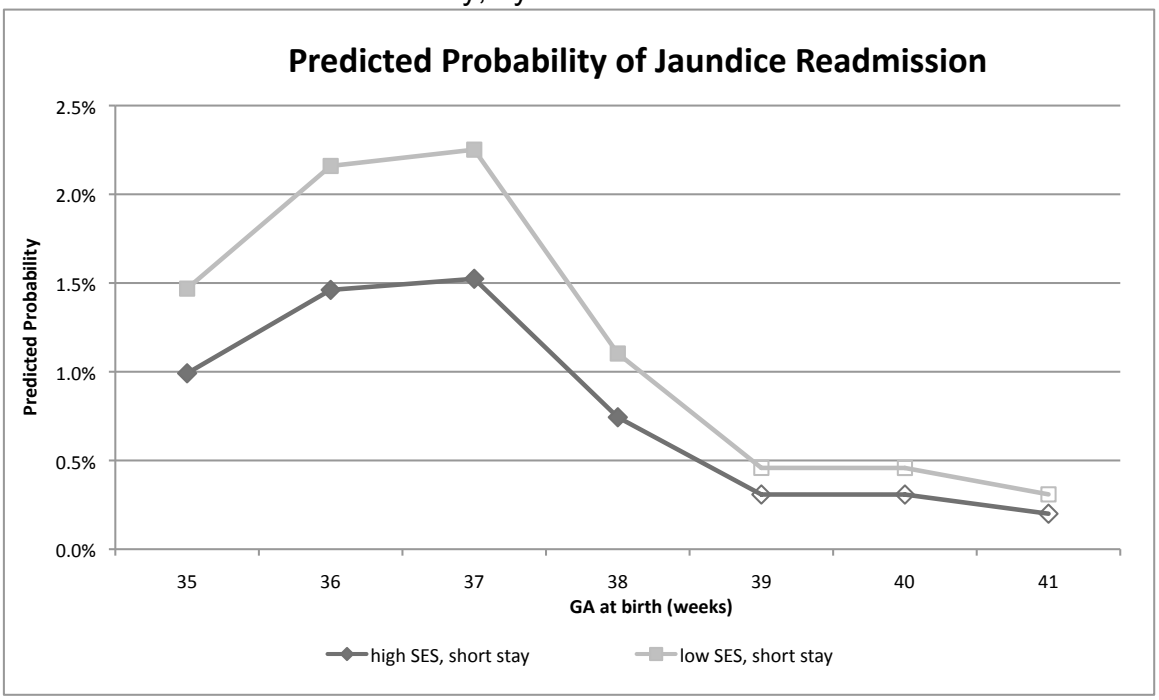
Readmissions for jaundice demonstrated a slightly different pattern from the other models (see Table 6, column 1). The interaction of short stay and gestational age was not significant (p=0.60). Short stay was significant as an independent variable with an OR=2.4 [1.6-3.6], translating roughly to relative risk,[38] as the overall incidence of jaundice admissions was low at 0.7%. No 34 week infants were admitted for jaundice. Being breastfed at initial birth discharge increased the risk of readmission, with an OR=6.1 [2.9-12.5]. Predicted probability for short stay infants is depicted in Figure 5, only short stay infants are depicted as non short stay infants were rarely readmitted for jaundice. Inspection of the probability graph reveals increasing probability of admission until 37 weeks and then a tapering off of risk as gestation increases. Low SES was associated with a 50% increased risk of admission when compared to high SES. Also demonstrating high increased odds of admission in this model were primiparity, and jaundice in the birth hospitalisation (See Table 6, column 1)

Table 6: Odds ratios with confidence intervals for included independent variables, models without significant interactions, by reason for admission at up to 28 days of age

Variable	jaundice n=172		all other n=402	
	OR	95% CI	OR	95% CI
maternal diabetes	1.4	0.9-2.4	0.9	0.6-1.4
primiparity	**1.4**	1.0-1.9	**1.6**	1.3-2.0
maternal age group	p=0.78		p=0.06	
<19 vs 19-34	1.0	0.5-2.0	0.6	0.4-1.0
>34 vs 19-34	1.2	0.8-1.8	1.3	0.9-1.7
ventilation	1.3	0.3-5.6	1.2	0.7-2.0
male sex	0.9	0.7-1.3	**1.8**	1.4-2.2
birth morbidity	**2.2**	1.4-3.7	**2.7**	2.1-3.7
any SCU stay	0.6	0.3-1.1	1.1	0.8-1.6
congenital anomaly	0.8	0.3-2.1	**10.3**	7.8-13.7
rural residence	**1.6**	1.2-2.2	**1.8**	1.4-2.2
jaundice	**2.7**	1.6-4.7		
any breastfeeding	**6.1**	2.9-12.5	**0.6**	0.5-0.7
short stay	**2.4**	1.6-3.6	**2.4**	1.8-3.1
income group				
low vs middle	1.4	0.9-2.0	0.8	0.7-1.1
low vs high	**1.5**	1.0-2.2	1.2	0.9-1.6
middle vs high	1.1	0.7-1.6	**1.5**	1.1-1.9
Gestational Age (weeks)				
34	NE	NE	1.5	0.7-3.2
35	**3.2**	1.3-8.4	**2.4**	1.3-4.4
36	**4.8**	2.5-9.2	1.4	0.8-2.6
37	**5.0**	3.1-8.2	1.5	0.9-2.3
38	**2.4**	1.5-3.9	1.3	0.9-1.9
39	1.0	0.6-1.7	1.3	0.9-1.8
40	REF		REF	
41	0.7	0.3-1.3	1.1	0.8-1.5

significant OR in bold, NE=no events, REF = reference group,

Figure 5: Predicted probability of a jaundice readmission at up to 28 days of age, for reference infant with short stay, by GA and SES



Points where GA is significant vs. 40 weeks are filled, non-significant are open

All other Diagnoses:

This group did not demonstrate an interaction between short stay and GA, and in fact only demonstrated a significant effect of GA for 35 week infants (See Table 6, column 2). Short stay was associated with increased odds of readmission, OR=2.4 [1.3-4.4]. Primiparity, male sex, birth morbidity, having a congenital anomaly or a rural residence increased the odds of readmission. This group includes those infants admitted with a congenital anomaly diagnosis, partially contributing to the large effect. Breastfeeding at newborn discharge was protective (OR=0.6 [0.5-0.7]). Being of middle compared to high SES increased the odds of admission, and being of low SES approached significance in increasing odds.

Discussion:

Gestational age, either alone or as an interaction with length of stay at birth hospitalisation, and socioeconomic status demonstrated significant effects on neonatal readmission in this cohort, even after controlling for the multiple confounding variables associated with low SES and prematurity.

Readmission risk decreased as GA increased with either a significant or suggested increase at 37 weeks in short stay infants, in all but the 'all other diagnoses' model. The most dramatic evidence of this was seen in short stay 36 and 37 week infants, where relative to 35 week infants, their risks were increased by 50% to be readmitted for jaundice. As discussed in detail further on, this could be due to different discharge practices in 'term' 37 week infants over late preterm 35 week infants. Increased readmissions in late preterm infants have been reported in the literature. A study of emergency department visits demonstrated that late preterm infants present at twice the rate expected from their population proportion to the emergency room.[39] Readmissions for jaundice in late preterm and term infants following a short stay are well documented in the literature.[21,22,24,28-30,39] Few of these studies however are population based, and none discriminate by week of GA. The inclusion of 37 week infants, demonstrated in this study to have an increased risk over late preterm infants, would bias those studies to the null, suggesting that in fact the risks of readmission in late preterm and early term infants may be more than is currently believed. The lack of an effect seen in the 'all other diagnoses' model may be due to the heterogeneity of diagnoses and the capture of the majority of maturity-related morbidity in the remainder of the models. Infants admitted with poor feeding were included in that

model but make up a small (17%) proportion. Our rates of feeding related issues compare with the 8-10% reported in the literature.[28, 39]

The importance of length of stay is demonstrated in all models and its greater impact on late preterm infants is demonstrated in the overall admission model where it was associated with a variable increased risk of admission from 2-13 times. It also had a greater effect on late preterm infants in the respiratory model. While we did not examine the individual admission diagnoses, some respiratory admission would be for apnea or irregular breathing, which may not present until after the first two days of age, and thus during the initial stay. This supports the guidelines recommending these infants not be considered for early discharge,[40-42] or if they are discharged early, ensure that breastfeeding is established[22] and close follow-up is ensured.[25, 43] Interesting in both these models is the higher risk a short stay poses to 37 week infants over 36 or 38 week infants. With growing recognition and education surrounding the risks of late preterm birth these infants may undergo greater scrutiny prior to discharge with a lower threshold for keeping them admitted. Infants at 37 weeks are considered term and might be discharged without this scrutiny but due to innate differences in maturity many infants will not act as term infants. All infants should have good follow-up in the community, individualized for each infant with an emphasis on those discharged early. Markers of physiologic maturity over strict GA based guidelines are important when assessing individual patients for discharge and should avoid readmissions caused by too early discharge, or inadequate follow-up in the community.

In the models where short stay acted independently of GA it more than doubled the odds of admission, in keeping with the published literature. One study of late preterm infants demonstrated 33-36 week infants with stays less than 4 days at birth accounted for 9% of the discharges, but 19% of admissions,[26] with an OR=2.94 [1.87-4.62] versus short stay term infants, and no increased risk when late 33-36 week infants with longer stays were compared to term. Another study did not demonstrate an association with length of stay in NICU discharged infants[30] however it only examined late preterm infants who stayed less than 5 days. Studies of NICU discharged infants represent only a subset of our cohort, and an NICU stay itself may be protective for readmission,[25] as was seen in our study for respiratory readmissions and suggested for 'any admission'. Similar to our study, a study by Tomashek et al[29] demonstrated double the risk of readmission in short-stay preterm infants over term infants, and another study in well-term and late preterm infants[28] demonstrated a length of stay of less than 72 hours predictive of readmission for jaundice.

Compounding the innate risks of prematurity and variable physiologic maturity is the effect of socioeconomic status. This study demonstrated that low SES increased the odds of readmission by up to 50%, exerting more of an effect than traditional medical variables frequently controlled for such as maternal age and parity. The increased risk of prematurity in low SES mothers is well documented[1,10-16,29,44,45] but whether these infants are at increased risk after their preterm birth is relatively unstudied. In an earlier paper (Chapter 4) we have demonstrated that they have increased birth hospitalisation morbidity, and now the effect of low SES is demonstrated to be larger after birth discharge. Infants

born to Aboriginal mothers of low SES have shown increased readmissions in their first 28 days.[46] A study by Martens et al[12] of neonatal readmissions in the same database as ours, has demonstrated over a doubling of neonatal readmissions in low versus high income quintile infants. Our lower effect of SES could be explained by control for more potential confounders, as the study by Martens et al only controlled for maternal age, LBW status, prematurity (<37 weeks) and CS delivery. Interestingly this study did not demonstrate an effect of maternal length of stay. Another study reporting on data from an Ontario postpartum experiences survey reported no effect of length of stay on admission rates but a significant association with a non-employment related income source and low maternal perceived health and support status.[47]

The elucidation of the complex relationship between length of stay, gestational age and socioeconomic status is important for many reasons. In order to meet the increasing and often complex health care needs of these babies and their families information is needed on what this entails and how best to provide it. Studies should ensure that they separate the prenatal effect of SES, its impact on preterm birth and abnormally high or low birthweight, from its postnatal effects discrete from those linked to GA and weight at birth. Information within the context of universal access to health care is important, as type of insurance and lack of access are associated with poorer outcome in American studies.[30,48] Education and support programs targeted at young mothers[32,49] have been proven effective for improving perinatal health including reducing readmissions. Research should be undertaken, and programs put in place to see if these effects can be extended to all families of low SES. Educational initiatives such as the

AWOHN[50] late preterm infant initiative that is currently ongoing, aim to educate health care providers and parents alike in the management of these infants. Central to these programs is the emphasis on establishment of feeding, monitoring for jaundice and good postpartum follow-up for both mother and infant.

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Chapter 6: Post-Neonatal Admissions

Children in families of low socioeconomic status (SES) are well documented to have poorer health than higher SES children, and one measure of this is hospitalisation rates.[1-21] The exact pattern and estimates of effect vary with measures of SES used, patient population, and control for confounders. The prevalence of medical confounders, especially prematurity, varies with SES[22-24], and this is not always accounted for in studies of hospitalisation outside the newborn period. The upper age limit for population-based samples is variable, and it is rare for those looking at infancy specifically to differentiate between neonatal readmissions and those over the remainder of the first year of life. Studies focusing more on contributions of prematurity often are restricted to certain admission types or extreme prematurity, with variable control for SES. Thus it is unclear if the increased risk of hospitalisation in infancy for low SES infants is due to SES or the association of low SES with prematurity.

There are many reasons to postulate that it is both low SES and prematurity which are responsible for the increased hospitalisation risk in these infants. Low SES mothers are less likely to have social support, less likely to have a stable living environment and food security, less likely to breastfeed and more likely to experience postpartum depression, smoke cigarettes and have higher levels of both measured and perceived stress,[22,25,26] all of which increase infant hospitalisation.[4,9,12,16,18] Studies of hospital usage within a universal coverage model such as Canada are important to avoid confounding by availability of insurance or care access, though barriers to effective care still exist

regardless of universal health care coverage, due to distance and language barriers.

Prematurity is also recognized as a risk factor for hospitalisation over the first year of life with most literature focused on the extremely low birth weight population or specific disease subgroups such as respiratory syncytial virus (RSV). Low socioeconomic status is a risk factor for preterm birth,[26-29] and thus it is often controlled for as a confounder, but not primarily investigated in studies of ex-premature infants. This study aims to look at the impact of both factors, SES and prematurity in a population based cohort of infants born at 34 to 41 weeks gestational age(GA). Late preterm infants, those born at 34 to 36 weeks GA, are the topic of current research due to their proportionally large numbers and increasing birth rate. The majority of studies focus on mortality or early morbidity within the newborn period, all of which are increased over term infants (see Chapter 4-5). Whether this risk extends into the first year of life, and the relative contributions of medical and socio-demographic risks are unclear. There is emerging evidence that late preterm birth can lead to poorer developmental and school outcomes[30-32] as well as respiratory morbidity,[5,33] and the question is whether this risk extends into other disease areas as well, and how it is modified by SES.

Methods:

A retrospective cohort study was undertaken utilizing data housed at the Manitoba Centre for Health Policy (MCHP). The Population Health Research

Data Repository (Repository) at the MCHP contains a number of anonymized administrative datasets maintained by Manitoba Health. This study utilized data from hospital discharge abstracts, Vital Statistics, and population registry data as well as public access Canada Census files and data from Family Services. The results and conclusions are those of the authors and no official endorsement by the providers of the data is intended or should be inferred. The Repository contains information on almost all residents of Manitoba, with the exception of RCMP officers, inmates of federal penitentiaries and members of the Canadian Armed Forces. Appropriate approvals were obtained from the custodians of all information sources in addition to the University of Manitoba Health Research Ethics Board and the Health Information Privacy Committee of Manitoba.

The cohort includes all infants born at 34 to 41 completed weeks gestation during the fiscal years 2004/2005 to 2005/2006, who remained in Manitoba until their first year birthday. It also includes the linked maternal file for extraction of pregnancy related variables. The initial dataset contained 25 834 newborn records that were matched with population registry (22 unmatched) and maternal health records (2 unmatched) successfully for 25 810 infants. Of these, 436 moved before their first birthday and 62 were missing essential demographic data (birth weight, GA or income data) and were removed from the analysis, thus resulting in a final cohort of 25 312 infants. Income and gestational age distribution of those infants who moved did not differ significantly from those retained in the sample (see Chapter 2). The dataset of admissions (after initial birth hospitalisation) initially contained 4 467 records. These were further classified into 3 993 discrete hospitalisations, after inter-hospital transfers were

merged into one admission. Infants classified as boarder infants, that is, those infants admitted to accompany another requiring care, usually their mother, not due to their own illness, were not included in the analysis, they constituted 323 of the admission episodes, leaving a total of 3 670 admission episodes in infants up to 365 days of age. Counts of admissions were generated from these records and merged to the mother-infant pair records.

Two different variables were used to assign infants to an SES group using maternal data. An individual level variable, receipt of provincial income assistance by the mother in the month of delivery, placed an infant in the lowest SES group. Area-level income information on average household income from Canada Census data was aggregated at the dissemination area level (approximately 400 persons) and grouped into population quintiles. Income quintiles were used to place the infants not on income assistance into one of the three groups. Infants in income quintile 1 were placed in the lowest group along with the income assistance recipients; quintiles 2 and 3 were placed in the middle group, and quintiles 4 and 5 in the highest group.

Maternal Variables:

Maternal codes taken from the hospital record included maternal age (years) and parity. The presence of maternal diabetes was established using maternal ICD10[34] codes from the hospital abstract. There was no distinction made between types of diabetes, as insufficient clinical data on the maternal history is available from the database. Rural location is defined by postal codes outside of Winnipeg or Brandon on the maternal record. Receipt of income

assistance was taken from the Manitoba Family Services and Consumer Affairs, Employment and Income Assistance database.

Newborn Variables:

GA was taken from the maternal hospital record and would be based on menstrual dates or ultrasound dating unless the clinical estimate at delivery differed in the opinion of the physician of record. Infant gender, birth date, birth weight, breastfed or not, and length of initial birth stay are taken from the newborn record. Some composite variables, reflecting newborn complications include birth morbidity, need for ventilation, or special care unit (SCU) admission are retained from an earlier study of birth hospitalisation outcomes. Birth morbidity includes both major and minor complications experienced during the birth hospitalisation. Further details of these variables can be found in Chapter 4. Infants are classified as having a congenital anomaly (CA) if they received a diagnostic code at any time during that year from the significant congenital anomalies group (see Appendix 1).

Hospital admissions in this study are those occurring from 29 to 365 days of age. Neonatal readmissions were examined in another study, reported in Chapter 4. The 'most responsible diagnosis' from the first episode in the encounter is assigned as the reason for admission. ICD 10 codes utilized in the following categories are found in Appendix 1. Unless otherwise indicated, all results are for any admission within the category, infants with multiple admissions within the same category are only represented once.

Five categories of hospital admissions were examined initially, but not all were modelled or reported individually due to sample size constraints:

1. **Respiratory**: both infectious and non-infectious causes of respiratory illness

2. **Infection**: includes all non-respiratory infections, viral or bacterial including but not limited to septicemia, urinary tract infections/urosepsis, gastro-intestinal infections, cellulitis and meningitis. It includes those infants admitted with fever to rule out sepsis.

3. **Congenital Anomaly**: includes those infants for whom the most responsible diagnosis is from the 'significant congenital anomaly' codes specified previously.

4. **Injury**: those infants admitted for care of accidental or non-accidental injury, including poisoning and thermal injuries.

5. **All other**: Any infants for whom the 'most responsible diagnosis' is not found in the above groups

Regression models were constructed to control for the effect of other perinatal variables. GA was entered as a classed variable with 40 weeks as the reference. Maternal age was entered as a categorical variable with three groups (<19, 19-34 and >35 years), with 19-34 years used as the reference. SES was analyzed using the income groups previously described with highest as the reference. The remainder of the variables were binomial. Logistic regression models with admission as a binomial outcome were initially run with an

interaction variable for SES and GA but the interaction was dropped if not significant. Significance was set at $p<0.05$. All data handling and statistical analysis was done using SAS version 9.1 for Unix.[35] For predicted probability comparisons, a reference infant was defined as born to a multiparous mother without diabetes, from the 19-34 year age group. The reference infant was female, breastfed at initial birth discharge, without congenital anomalies, living in an urban setting and did not experience birth morbidity, SCU admission or ventilation.

Results:

For characteristics of the sample please see Tables 1-2. Of the 25 312 infants in the birth cohort, 6.1% (n=1524) were born preterm at 34 to 36 weeks GA. There were 2073 infants (8.2%) who experienced at least one admission from 29-365 days of age, with 10.5% of admitted infants (n=218) being preterm. This results in an overall admission rate of 14.2% for preterm infants, and 7.8% for term infants. Almost half, 49.5% (n=1026) of admitted infants were from the lowest SES group. Admissions increased with decreasing GA (see Figure 1) and with decreasing SES (see Figure 2). Preterm infants accounted for a larger proportion of admissions than their population percentage in all groups. Respiratory admissions formed the largest group, followed by the 'other' group

Table 1: Characteristics of study population by GA at birth and selected maternal and neonatal variables

GA	34	35	36	37	38	39	40	41
n	276	457	801	1780	4189	6535	7218	4056
Maternal Characteristics								
maternal age group, years								
<19	5.8	3.5	4.2	4.9	4.4	5.4	5.1	5.5
19-34	80.4	81.2	78.0	79.0	80.5	82.2	83.5	83.3
>34	13.8	15.3	17.7	16.1	15.1	12.4	11.4	11.2
primiparous, %	44.2	39.6	36.6	35.7	32.5	35.1	39.4	46.8
CS, %	35.9	33.7	29.0	24.9	30.1	21.2	13.9	17.2
induced delivery	26.8	35.2	35.0	33.7	34.8	22.1	16.4	39.1
multiple birth	23.6	21.9	11.7	8.0	2.7	0.3	0.2	0.0
maternal diabetes	7.6	12.0	17.2	10.1	8.5	3.8	2.4	0.8
low SES	35.9	37.2	39.3	36.8	33.6	31.8	31.2	30.4
Newborn Characteristics								
male, %	58.0	55.4	54.2	51.7	53.0	49.6	50.1	51.9
mean BW, grams (SD)	2377 (460)	2640 (534)	2936 (530)	3143 (480)	3358 (479)	3496 (459)	3656 (463)	3774 (469)
BW range	1184-3902	1216-4599	1420-5160	1172-5305	1610-6440	1703-6457	1349-5589	1438-5795
median LOS (range)	13 (1-90)	6 (1-66)	3 (1-71)	2 (1-103)	2 (1-168)	2 (1-93)	2 (1-55)	2 (1-42)
any neonatal morbidity, %	85.5	62.4	45.3	23.4	17.6	11.6	11.6	12.1
major congenital anomaly, %	10.1	5.7	5.6	3.2	3.1	2.1	1.7	2.1
short stay, %	7.3	11.8	28.2	56.7	61.3	70.9	74.9	70.6

Please see text for description of variables, CS=cesarean section, SES=socioeconomic status, BW=birthweight, LOS=length of stay

and then infection related hospitalisations, congenital anomalies and injuries (see Figure 3). In this Figure infants may be represented in multiple categories if they had more than one type of admission, but not more than once within a category.

Table 2: Characteristics of study population by SES and selected maternal and newborn characteristics

SES group	lowest	middle	highest	chi-sq
n	8203	8854	8255	
Maternal Characteristics				
maternal age group, yrs <19	10.3	3.3	1.7	p<0.0001
19-34	81.6	83.7	80.8	p<0.0001
>34	8.1	12.9	17.5	p<0.0001
primiparous, %	33.3	40.2	40.6	p<0.0001
CS, %	17.5	21.9	23.0	p<0.0001
maternal diabetes	7.2	4.2	3.0	p<0.0001
induced delivery	25.5	27.9	26.9	p=0.0014
multiple birth	1.7	2.0	2.8	p<0.0001
rural	45.8	44.5	42.3	p<0.0001
Newborn Characteristics				
male, %	51.3	51.4	51.0	p=0.7066
mean BW, grams (SD)	3482 (554)	3505 (534)	3492 (526)	
BW range	1216-6208	1172-6457	1331-5746	
median LOS (range)	2 (1-103)	2 (1-168)	2 (1-51)	
premature	7.1	5.4	5.7	p=0.0001
any neonatal morbidity, %	17.7	17.2	14.0	p<0.0001
major congenital anomaly, %	2.8	2.6	2.1	p=0.0046
short stay, %	67.0	65.3	66.6	p=0.0559

BW=birthweight, CS=cesarean section, LOS=length of stay, SES=socioeconomic status

Figure 1: Percentage of infants, by GA at birth, with any hospital admission from 29 to 365 days of age

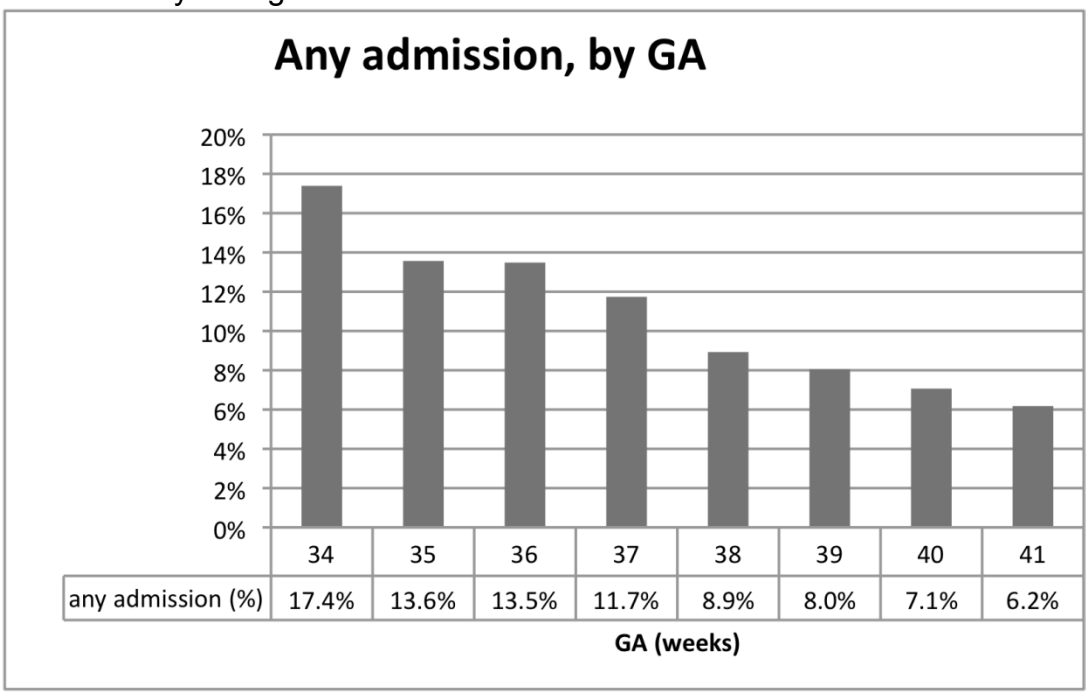


Figure 2: Percentage of infants, by maternal SES group, with any hospital admission from 29 to 365 days of age

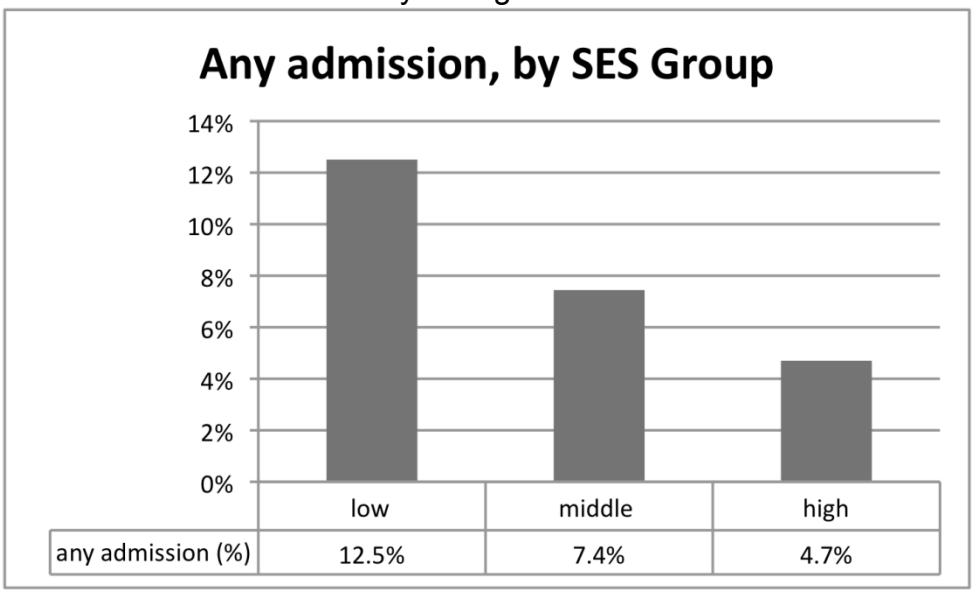
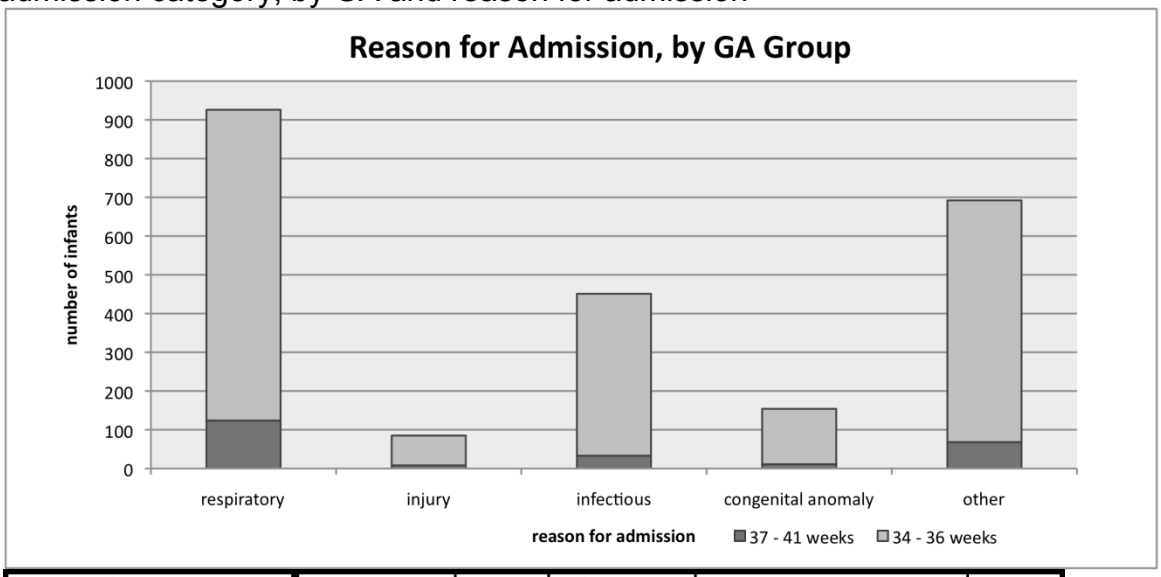


Figure 3: Number and percent of infants with at least one admission in an admission category, by GA and reason for admission



reason for admission	respiratory	injury	infectious	congenital anomaly	other
any admission					
37 - 41 weeks	802	77	418	143	624
34 - 36 weeks	124	8	33	11	68
% of infants	3.7%	0.3%	1.8%	0.6%	2.7%
% of admitted infants	44.7%	4.1%	21.8%	7.4%	33.4%

Infants are represented only once within a category, but may be represented in multiple categories, thus totals are greater than 100%.

Regression results:

Table 3: Results of the regression models by reason for admission
**interaction of SES and GA significant see text, and Tables 4-5.

	any admission (n=2073)		respiratory (n=926)		Infectious (n=451)		all other (n=875)	
Variable	**OR**	95% CI	**OR**	95% CI	**OR**	95% CI	**OR**	95% CI
maternal diabetes	**1.2**	1.0-1.5	1.0	0.7-1.3	**1.5**	1.0-2.1	**1.5**	1.1-2.0
primiparity	**0.7**	0.6-0.8	**0.4**	0.4-0.5	0.9	0.8-1.2	0.9	0.8-1.0
maternal age group								
<19 vs 19-34	**2.0**	1.7-2.4	**2.9**	2.3-3.6	**1.7**	1.3-2.4	1.2	0.8-1.6
>34 vs 19-34	**0.7**	0.6-0.9	**0.6**	0.5-0.8	0.8	0.5-1.1	0.8	0.6-1.0
ventilation	1.1	0.7-1.6	1.2	0.8-2.1	0.3	0.1-1.0	1.2	0.7-1.9
male sex	**1.4**	1.3-1.5	**1.3**	1.1-1.5	**1.3**	1.1-1.5	**1.6**	1.4-1.8
birth morbidity	1.0	0.8-1.2	1.1	0.9-1.3	0.9	0.7-1.3	0.9	0.7-1.2
any SCU stay	**1.2**	1.0-1.5	**1.4**	1.0-1.8	0.8	0.6-1.2	**1.2**	1.0-1.6
congenital anomaly	**9.7**	8.0-11.8	**2.0**	1.5-2.8	**5.8**	4.1-8.3	**19.9**	12.9-24.9
rural residence	**1.7**	1.6-1.9	**2.6**	2.2-3.0	**1.5**	1.2-1.8	**1.2**	1.0-1.3
any breastfeeding	**0.6**	0.5-0.7	**0.6**	0.5-0.7	**0.6**	0.5-0.7	**0.7**	0.6-0.8
income group								
low vs middle	**1.5**	1.3-1.7	**		**		**1.2**	1.0-1.4
low vs high	**2.2**	1.9-2.5					**1.3**	1.1-1.5
middle vs high	**1.5**	1.3-1.7					**1.1**	0.9-1.3
GA (versus 40 weeks)								
34	**1.8**	1.2-2.7					1.2	0.6-2.1
35	**1.5**	1.1-2.0					1.0	0.6-1.8
36	**1.6**	1.2-2.0					**1.5**	1.0-2.3
37	**1.6**	1.3-1.9					**1.6**	1.2-2.2
38	**1.2**	1.0-1.3					1.2	0.9-1.6
39	**1.1**	1.0-1.3					**1.5**	1.2-2.0
41	0.8	0.7-1.0					1.1	0.9-1.5

Any admission:

In this model the interaction of GA and SES was not significant (p=0.08). Please see column 1 of Table 4 for results of the model. Late preterm infants had an increased odds of admission, from almost doubled at 34 weeks (OR=1.8 [1.2-2.7]), falling to an over 50% increase at 36 (OR=1.6 [1.2-2.0]) to 37 (OR=1.6 1.3-1.9]) weeks and remaining significant until 39 weeks (OR=1.1 [1.0-1.3]). The effect of SES was dramatic with an over doubled odds of 2.2 [1.9-2.5] for low versus high and a 50% increase as each income group improved, OR=1.5 [1.3-

1.7] for low versus middle and middle versus high. Multiple other variables were significant with maternal diabetes, maternal age less than 19 years, male sex, having a congenital anomaly, SCU stay at birth and rural residence increasing the odds. Having a mother greater than 34 years of age, a primiparous mother, or being breastfed at time of hospital discharge decreased the odds of admission.

Respiratory Admissions:

In this model the interaction between SES and GA was significant (p=0.02). In low SES infants until 37 weeks increased odds of admission were seen, except at 35 weeks, with no effect of GA in older low SES infants. In high SES infants prematurity increased the odds of admission until 37 weeks, at a higher magnitude of effect than that seen in low SES infants. Please see Table 4 for OR of the interaction.

Table 4: Odds Ratios for the interaction of GA, SES and Respiratory Admissions from 29 to 365 days of age

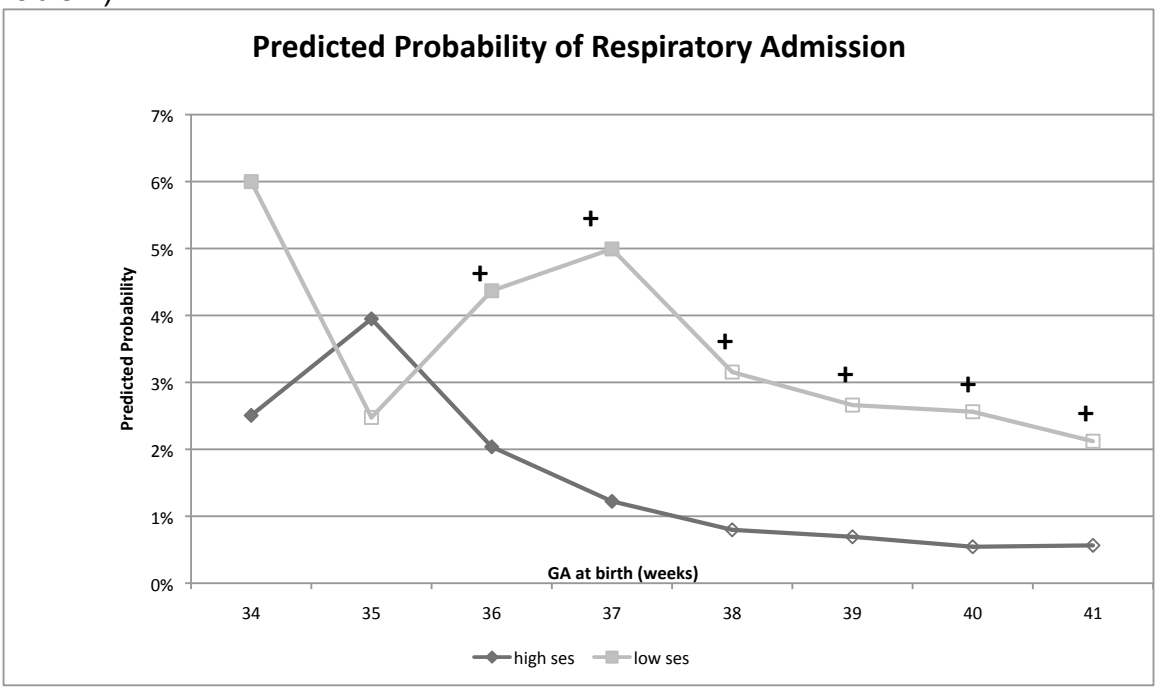
Effect of SES at each GA	OR	95% CI
34: low vs high	2.5	0.8-7.3
35: low vs high	0.6	0.3-1.5
36: low vs high	**2.2**	1.0-4.8
37: low vs high	**4.2**	2.2-8.2
38: low vs high	**4.1**	2.4-6.9
39: low vs high	**3.9**	2.5-6.2
40: low vs high	**4.8**	3.0-7.7
41: low vs high	**3.8**	2.0-7.2

Effect of GA at each level of SES	OR	95% CI
low: 34 vs 40	**2.4**	1.3-4.4
low: 35 vs 40	1.0	0.5-1.8
low: 36 vs 40	**1.7**	1.1-2.7
low: 37 vs 40	**2.0**	1.5-2.7
low: 38 vs 40	1.2	0.9-1.6
low: 39 vs 40	1.0	0.8-1.3
low: 41 vs 40	0.8	0.6-1.2
high: 34 vs 40	**4.7**	1.7-13.3
high: 35 vs 40	**7.5**	3.4-16.5
high: 36 vs 40	**3.8**	1.7-8.5
high: 37 vs 40	**2.3**	1.1-4.7
high: 38 vs 40	1.5	0.8-2.8
high: 39 vs 40	1.3	0.7-2.3
high: 41 vs 40	1.0	0.5-2.1

For ease of interpretation a graph comparing the predicted probability of admission by GA and SES can be seen in Figure 4. For term infants when low

SES was compared to high SES there was an approximately four-fold increase in predicted risk. Infants born at 37 weeks had the highest probability change from low SES. The effect of SES on late preterm infants was less marked but still present, and with the exception of the 35 week infants it caused an approximate doubling from low to high. Other factors associated with significantly increased odds were having a young mother (<19 years of age), male sex, an SCU stay at birth, rural residence and a congenital anomaly. Having a primiparous or older mother (>34 years of age), or being breastfed at hospital discharge decreased the risk of admission. Please see column 2, Table 4 for these results.

Figure 4: Predicted Probability of Respiratory Admission from 29 to 365 days of age, for reference infant, by GA and SES, significant difference versus 40 weeks solid data points, $^{+}$significant difference versus high income group (see also Table 4)



Infection related admissions:

In this model the interaction of SES and GA was significant at p=0.01. There was again demonstrated an increased effect size in the association

between low SES and admission at term gestations, with low SES increasing risk from 38 weeks and above, and no significant effect below that. Please see Table 5 for odds ratios of the interaction. In low SES infants there was no association with GA. For high SES infants however, 36 and 38 week infants had a significantly increased odds of admission over 40 week infants. For ease of interpretation a graph of the predicted probability of admission by SES and GA for a reference infant is seen in Figure 5.

Figure 5: Predicted Probability of an Infection Related Admission from 29 to 365 days of age, for reference infant, by GA and SES, significant difference versus 40 weeks solid data points, $^{+}$significant difference versus high income group (see also Table 5)

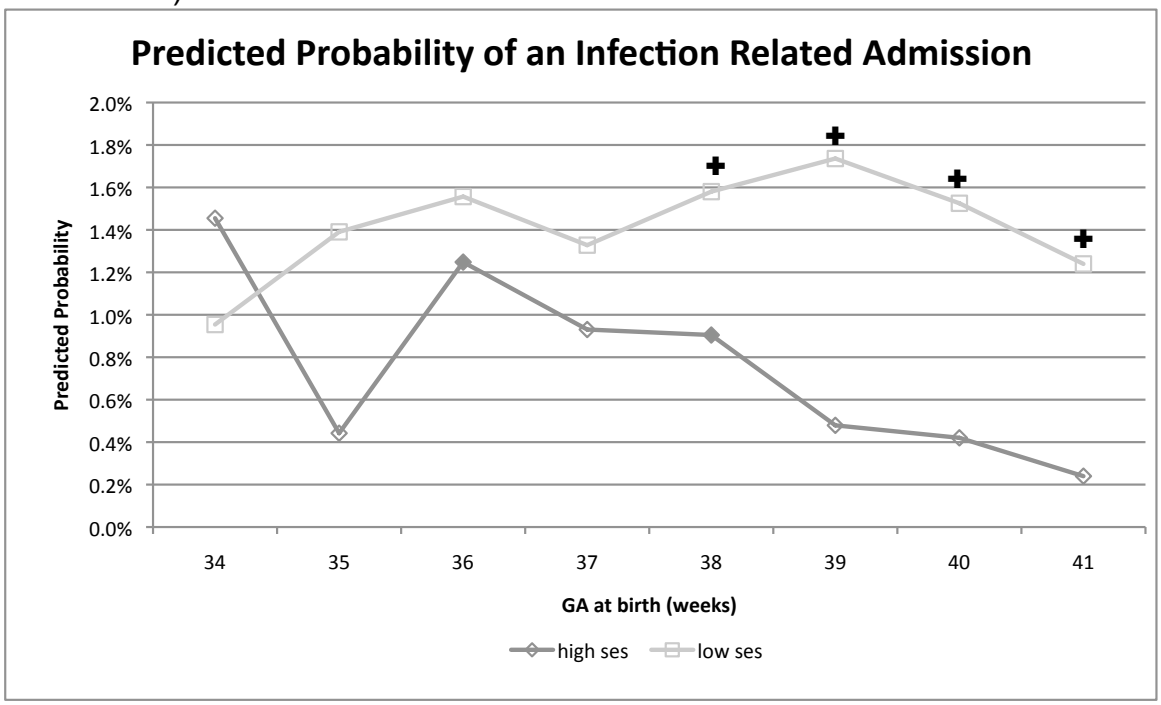


Table 5: Odds Ratios for the interaction of GA, SES and Infection Related Admissions from 29 to 365 days of age

GA (weeks) : income group comparison	OR	95% CI
34: low vs high	0.7	0.1-4.8
35: low vs high	3.2	0.4-28.0
36: low vs high	1.3	0.4-3.7
37: low vs high	1.4	0.6-3.4
38: low vs high	**1.8**	1.0-3.1
39: low vs high	**3.6**	2.0-6.3
40: low vs high	**3.7**	2.1-6.5
41: low vs high	**5.2**	2.0-13.6

income group: GA (weeks) comparison	OR	95% CI
low: 34 vs 40	0.6	0.1-2.7
low: 35 vs 40	0.9	0.3-2.4
low: 36 vs 40	1.0	0.5-2.0
low: 37 vs 40	0.9	0.7-1.5
low: 38 vs 40	1.0	0.7-1.5
low: 39 vs 40	1.1	0.8-1.6
low: 41 vs 40	0.8	0.5-1.3
high: 34 vs 40	3.5	0.8-16.2
high: 35 vs 40	1.1	0.1-8.2
high: 36 vs 40	**3.0**	1.1-8.4
high: 37 vs 40	2.2	0.9-5.3
high: 38 vs 40	**2.2**	1.1-4.3
high: 39 vs 40	1.1	0.6-2.3
high: 41 vs 40	0.6	0.2-1.6

In addition to these effects, maternal diabetes, having a younger mother, male sex, having a congenital anomaly, and being from a rural residence increased the odds of admission. Being breastfed at hospital discharge decreased the odds. Please see Table 4, column 3 for these results.

All other admissions:

In this group the interaction between SES and GA was not significant (p=0.81). GA exerted a modest effect with elevated odds at 36 (OR=1.5 [1.0-2.3]), 37 (OR=1.6 [1.2-2.2], and 39 (OR=1.5 [1.2-2.0]) weeks when compared to 40 weeks, with somewhat wide confidence intervals. SES was associated with an effect in all comparisons; up to a 30% increase in odds of admission for low SES infants compared to high SES infants (OR=1.3 [1.1-1.5]). As this outcome included infants admitted for management of congenital anomalies, including various surgical procedures, the OR for congenital anomalies was high at 19.9

[15.9-24.9]. In addition maternal diabetes, male sex, rural residence and an SCU stay at birth increased the odds. Breastfeeding at time of hospital discharge decreased the odds. Please see Table 4, column 4 for these results.

Discussion:

Both gestational age and socioeconomic status affect risk for hospitalisation in the first year of life with a varying strength of association depending on reason for admission. The interaction of SES with GA however, in two of the most common admission types in infancy, underlines the importance of considering the two variables together in any study of risk factors for admission. Term infants are not subject to the inherent risk of admission associated with prematurity, yet if of low SES their predicted risks are similar to those of preterm infants. Conversely, preterm infants have high risk from their gestation and any added risk due to low SES only increases it further.

A pattern can be seen when comparing the associations of GA and SES for the two largest groups, respiratory and infection related admissions. In high SES infants there was a residual increased risk from preterm birth, but in the low SES infants this is overshadowed by the risk due to poverty. For respiratory admissions the effect of GA persisted, but with lower odds than that seen in high SES infants, and for other infection related admissions the effect of GA is not seen. It is uncertain if in a larger sample the risks would persist at low level, further investigation is needed.

There is little population-based literature on hospitalisation risk overall in late preterm infants, and no literature found that reports risk by week of GA. A

very recent study from McLaurin et al[36] reported admission data from a patient database of commercially insured American patients. They reported admissions in late preterm and term infants from over 15 days of age until one year. They demonstrated a 6.8% rate for term infants and a 12.1% rate for late preterm infants, in addition to higher mean care costs of $4069 for term infants versus $12247 for late preterm infants. Our rates are slightly higher, but similar in distribution, and it is difficult to know if the cohorts are comparable. The socio-demographic and individual GA distribution was not reported, and few perinatal factors other than length of stay in the newborn period were included. They did demonstrate that late preterm infants with a birth stay longer than 4 days were more likely (13.1% vs. 10.0%) to be admitted again, which would be a proxy for infant health at birth. It is the only other study that could be located looking specifically at all admissions outside the newborn period in late preterm infants. Other population-based studies report rates in all infants less than one year of age at 21.7%,[17] 14.7% for girls and 20.3% for boys,[2] and Quebec studies report rates up to 5 months of age at 12.3-12.9%.[12,20] These studies however do not control for GA at birth and include neonatal readmissions. One study which controlled for multiple social risk factors in infants up to 12 to 24 months of age did not demonstrate a significant effect of prematurity.[18] The remainder of population-based studies report on children up to 19 years of age[1,3,8,13,15,37] and are not comparable.

Higher risks in late preterm infants for neonatal readmission are well documented[38-41] but the persistence of this risk outside the newborn period is relatively unstudied in all but respiratory admissions. In addition our study

demonstrated increased risk not just for late preterm infants but also for all infants less than 38 weeks GA. Late preterm and early term infants differ from later term infants in maternal, fetal and newborn characteristics. This study controlled for many of these influences, yet still demonstrated an increased risk. This might imply subtle damage or derangement in the physiologic maturation that occurs during those few weeks the infant was born premature. There could be other variables unrelated to maturity but with disproportionate representation not controlled for in this analysis. While the precise clinical diagnosis may be of variable reliability in administrative data this method has demonstrated excellent reliability for capture of hospitalisation events.[42, 43] Further detail about early neonatal course, maternal risk factors and hospitalisation episodes could be gathered via linkage with clinical databases, and supplemented with prospective cohort studies. Further investigation into how maternal diabetes increases admission risk and whether improved antenatal management decreased risk could be implemented. Efforts to support and encourage breastfeeding especially in late preterm infants and those admitted to an SCU at birth should be continued.[44,45] The consistent association in this analysis between breastfeeding at discharge and reduced admissions bears further investigation. As information on continued breastfeeding is unavailable it is unclear if this represents a true effect, is a proxy for another variable or indicative of an infant characteristic that precludes or limits breastfeeding.

The most detailed knowledge about admission risk in late preterm infants is from the RSV studies. The interaction effect of GA and SES on respiratory admissions in this study, a large proportion of which would be expected to be

secondary to RSV, is in keeping with the published literature. Studies in late preterm infants have demonstrated a similar risk of hospitalisation as infants of 29-32 weeks GA[4,33] and twice that of term infants.[46] Some studies have demonstrated increased admissions in association with various measures of SES such as low maternal education,[5,19,46] or low income.[33] They have also demonstrated increased admissions in association with other variables intrinsically linked with SES such as daycare attendance, other children in the home, lack of breastfeeding, smokers in the home and being small for gestational age.[33] Studies of respiratory admissions, including but not limited to RSV, demonstrate the same elevated risk based on low maternal education, receipt of social assistance or single parent families with[14] or without[47] mentioning gestational age. This persistent elevated risk supports current practices of offering prophylaxis for RSV in the context of late preterm birth with risk factors. In our study for term infants the probability of admission almost quadrupled from high to low SES, as compared to a doubling at 34 and 36 weeks. This relatively higher impact of low SES in term infants is likely due to the intrinsically higher baseline risk for late preterm infants, due to residual physiologic effects of prematurity. The fact that low SES infants regardless of gestational age at birth experience higher respiratory admissions in this study highlights the need for comprehensive programs aimed at eradicating child poverty as a strategy to improve health in children, and improving outpatient and preventative care in this population. The association between young maternal age and respiratory admissions underlines the importance of support programs for young women

both to reduce first or subsequent births[48], and reduce admissions of infants born to young mothers.[49, 50]

The impact of SES is seen in other, non-respiratory admission groups in this study. For non-respiratory infection related admissions, being of low SES exerted a stronger relative effect than being of low GA. This effect of SES is in keeping with other published studies, not controlling for GA and including children up to 5 years of age, where gastroenteritis admissions were increased from double to almost 8 times in low SES.[7,10] This decreased GA effect in non-respiratory infectious admissions versus its strong effect in respiratory admissions, the majority of which are infectious, suggests underlying lung damage secondary to prematurity or adverse fetal effects such as smoking. The 'all other' admissions model had more variable diagnoses, and is hard to interpret in isolation. It included those children admitted for management of congenital anomalies, and other chronic conditions. In one Canadian study[11] children with 'complex chronic conditions' whilst similarly distributed across income groups, had a 24% higher risk of admission in the lowest compared to highest quintile and a higher risk of death. This raises the issue of how much of the excess hospitalisations in low SES children are from increased medical risk versus actual or perceived inability of the caregivers to manage the child at home or negotiate an outpatient management system. Ambulatory sensitive admissions, those that might have been prevented by timely outpatient care, are higher in low SES children[2] by approximately 50%.

This study was designed to evaluate two primary determinants of morbidity in infants, GA and SES. To do so it adjusted for multiple perinatal

variables that are disproportionately represented across these determinants. The strengths of this study include its population-based sample of all preterm and term infants of 34 to 41 weeks GA, in contrast to matched controls or a random sample from within a population, or population based on one care provider only. It included infants cared for in many different areas including rural and urban, community and tertiary care centres, normal newborn nurseries and intensive care nurseries. The lack of individual level markers of SES was overcome using area level data, which has previously been demonstrated as appropriate for assessing the association between SES and health outcomes.[42,51] Very few infants were lost due to non-linkage or lack of key data. Multiple perinatal variables were controlled for within the analysis. The major weakness of the study is the inherent risk of inaccuracy of coding of disease and morbidity in administrative data. The MCHP repository data has been utilized in the past and demonstrated good congruence with other published literature.[17,39] The results of this study are in agreement with the published literature, and robust across different outcome groups, suggesting that small errors in coding would not affect the results.

Programs to provide coordinated care to all infants and their families, including education, income and family support should be implemented as an overall strategy to improve child health. Those programs aimed specifically at infants in low SES environments are essential to reduce the impact of these admissions. Careful evaluation of planned programs for efficacy and acceptance are important and helpful to governments and policy makers. Low SES should be recognized as a risk factor for admission, at times exerting a greater effect than

the more traditional medical risk factors. This study joins the growing literature reporting that the risks of late preterm birth extend past the newborn period. Taken within the context of their increasing birth rate this lends a sense of urgency to further study and interventions to address both the roots of prematurity and poverty.

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Chapter 7: Conclusions and Future Directions:

This series of three studies within the same cohort of infants born at 34 to 41 weeks GA has demonstrated an association between GA, SES and morbidity in all time periods. The effect persisted after controlling for multiple confounding variables and for different types of hospitalizations. Whilst not always completely linear there is an overall impression of a gradient with morbidity increasing as SES or GA decreased, rather than a threshold at a certain gestation or income. The effect of GA was strongest in the immediate neonatal period and then decreased over the first year. Conversely, the association between SES and morbidity starts off small and increases in its effect size throughout the first year.

This study contributes to the literature in several ways. It confirms in a large, population based study the morbidity of both term and late preterm infants. It defines this by week of gestation, for a wide variety of diagnoses, and it reports its association and interaction with SES. As discussed previously, it is most commonly the effects of GA after control for SES which are reported in the neonatal period and the effects of SES after control for GA which are reported in the post-neonatal period. The unique effect of each throughout the first year emphasizes the importance of controlling for both factors in any research. The interaction of birth length of stay and GA for neonatal readmissions needs incorporation in to discharge practices and follow-up. The lack of a gradient for length of stay and GA in jaundice emphasizes good follow-up and possibly the importance of pre-discharge bilirubin screening for all infants, especially those in the higher risk zone in this study, 37 to 38 weeks. The suggestion that poverty

confers a relatively greater risk in term infants, at a magnitude approaching that of the effect of prematurity merits further study in a larger sample. The suggestion that low SES is associated with improved respiratory outcomes in some clinical situations is novel, and requires more precise clinical data for exploration, as the definition of RDS is difficult even in clinical cohorts. The consistent association between maternal diabetes and poor outcomes, along with its lack of an association with immediate neonatal respiratory morbidity requires further investigation, within a model controlling for SES. As this is a common comorbidity, increasing in worldwide prevalence, with potentially modifiable effects, there is a certain urgency to these investigations.

This information is essential for governments and policy makers to prioritize areas for resource allocation both for healthcare and for programs addressing socioeconomic differences. The gradient effect of GA emphasizes the importance of ensuring policies around neonatal monitoring; discharge and admission practices incorporate not only GA but markers of maturity, specifically as they pertain to 37 and 38 week infants. As this study utilized hospitalization as a marker of morbidity, further research into other aspects of healthcare provision is necessary to both complete the picture of resource usage as well as the fit between usage and need. Further research looking at the association between SES and morbidity, to establish causation and elucidate mechanisms is necessary to plan rational and effective strategies to combat the problem and to support those infants and families affected. Whether the associations in this study are true effects, or mediated through another confounder, such as smoking

or substance use, they increase in their effect size throughout the year, and addressing the modifiable risk factors early is essential and likely to be cost effective in the long run. Supplementation of administrative data with clinical databases, prospective cohort studies and qualitative studies of how SES mediates outcome is necessary to define the whole picture and ensure that all children, regardless of gestation and socioeconomic status have the best outcome possible.

Appendix 1: ICD 10 and CCI codes used in classifications

Table 1: ICD 10 codes for significant Congenital Anomalies (CA)

Significant Congenital Anomalies	E7-E9 (not E86-87, E84); Q0, 2 (not 2.11,2.50, 2.70), 30.0-30.1, 31-37, 39-45, 50-51
	Q52 (not 52.5), 56, 60-63, 71-75, 77-78, 79.0, 79.2-79.4, 79.8, 80-81, 82.0-82.4, 85-89, 9

Table 2: ICD 10 and CCI codes used to classify diagnoses received during the birth hospitalization

ICD 10 Codes for Birth Hospitalisation Morbidity	
Respiratory Distress Syndrome	P22.6
Other Respiratory Morbidity	J93; P14.2, 22.1, 22.8-22.9, 24-26, 28.0-28.1, 28.5, 29.3; R57
Other Complications of Prematurity	E86, 87; F982; P28.2-28.4, 74.1-74.2, 80-81, 92 (not 92.4)
Jaundice	P55, 57-59
Other Major Morbidity:	
Neurologic	G4; P20-21, 52, 90-91; R56
Infectious	A; B; P35-38, 39.3
Birth Injury	G54.0; J98.6; P10, 11.0-11.5, 12.0, 12.2, 13-14 (not 14.2), 15.0-15.3, 15.5-15.7
Cardiac	I42, 47-49, 51, 77; P29 (NOT P29.3), 83.2; Q21.1, 25.0; R00-01
Other	P50-51, 53, 56, 61.0-61.2
Gastrointestinal	P54.0-54.1, 75, 77, 76.0, 78.0-78.2, 96.1

CCI Codes for Resource Use	
Receipt of Phototherapy	1YZ12JADQ
Ventilation	1GZ31CAND, 1GZ31CRND, 1GZ38JANE, 1GZ31CBND

Table 3: ICD 10 codes used to classify 'reason for admission' during neonatal readmissions at up to 28 days of age or post discharge

Jaundice	R17 P55, 57-59
Respiratory	A15-16, 31.0, 36-37, 42.0, 43.0, 48.2 B01.2, 05.2, 06.8, 20.6, 25.0, 38.0, 38.1, 39.0, 40.0-40.1, 41.0, 42.0, 44.0-44.1, 45.0, 46.0, 59, 95-97 E84 J00-06, 09, 10.0-10.1, 11.1, 12-18, 17.1, 17.3, 20-22, 26, 32, 38, 39.0-39.1, 39.8 J 44.0, 44.8, 45-47, 85-86, 90, 93, 94.0, 95.0, 96.0-96.1, 96.9, 98, 99.8 P23, 25, 29.3 R06
Feeding	E46, 86-87 K21 P74, 92 R11, 62.8, 63
Infectious	G00-G08 H05.0, 60.0-60.1, 60.4, 65-7 I00-02 J10.8, 11.8 K12.2, 61, 65 L00-04, 05.0, 08, 30.3 M00-01, 72.6, 86 N10-12, 13.6, 15.1, 30, 34, 39.0, 43.1, 45, 48.1-48.2 P35-39, 81.9 R50 plus A or B but not in respiratory
Boarders	Z76.1-76.4

Table 4: ICD 10 codes used to classify 'reason for admission' in post-neonatal admissions at 28 to 365 days of age

Respiratory	A15-16, 31.0, 36-37, 42.0, 43.0, 48.2 B01.2, 05.2, 06.8, 20.6, 25.0, 38.0, 38.1, 39.0, 40.0-40.1, 41.0, 42.0, 44.0-44.1, 45.0, 46.0, 59, 95-97 E84 J00-06, 09, 10.0-10.1, 11.1, 12-18, 17.1, 17.3, 20-22, 26, 32, 38, 39.0-39.1, 39.8 J 44.0, 44.8, 45-47, 85-86, 90, 93, 94.0, 95.0, 96.0-96.1, 96.9, 98, 99.8 P23, 25, 29.3 R06
Infectious	G00-G08 H05.0, 60.0-60.1, 60.4, 65-7 I00-02 J10.8, 11.8 K12.2, 61, 65 L00-04, 05.0, 08, 30.3 M00-01, 72.6, 86 N10-12, 13.6, 15.1, 30, 34, 39.0, 43.1, 45, 48.1-48.2 P35-39, 81.9 R50 plus A or B but not in respiratory
Injury	V, W, S, T X0-8 Y0
Boarders	Z76.1-76.4