New Perspectives on Long Stay Patients in the Pediatric Intensive Care Unit: Definition, Characteristics and Impact.

by

Owen Woodger

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Abstract

For many children and their families, access to care in a pediatric intensive care unit (PICU) is vital. Unfortunately, as a rival good, it is also limited. This thesis analyzes the group which uses the most of this important and scarce good: long stay patients (LSPs). Using an original survey of PICU practitioners across Canada and an original dataset of a year of PICU admissions from a particular PICU, this thesis applies a unique mix of qualitative and quantitative methods to draw conclusions and generate hypotheses. Two findings are particularly noteworthy: a new theoretical framework for dichotomizing LSPs into “high-need” and “high-dependency” and the potential existence of “congestion effects” in which additional LSPs at any given time force PICUs to ration the care they can make available to any individual patient.

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List of Acronyms

AFT- Accelerated Failure Time

CHEO- Children's Hospital of Eastern Ontario

CCI- Chronically Critical Ill

ICU- Intensive Care Unit

LOS- Length of Stay

LSP- Long Stay Patient

PICU- Pediatric Intensive Care Unit

PH- Proportional Hazards

PRISM- Pediatric Risk of Mortality Score

ROC- Receiver Operator Curve

Introduction

Receiving high quality, timely health care can be the difference between health or sickness, pain or comfort, and even life or death. There are few settings where managerial and clinical decisions are more important for individuals' health, and wellbeing than in an intensive care unit. The added moral and economic importance of these decisions in a pediatric context make them even more pressing (Belli, Bustreo and Preker, 2005).

Therefore, this thesis examines the particular issue of long stay patients (LSPs) in the pediatric intensive care unit (PICU). LSPs in PICUs have been found to be at a greater risk of morbidity and mortality, and use significantly more resources than other patients, accentuating the need to understand this particular group (Naghib et al, 2010). Indeed, under the definition of LSPs used for this thesis, 8% of the patients use 41% of the total bed days. Applying empirical and theoretical economic practices to this group may generate important insights into how to better manage resources and deliver care in the PICU.

Given the clear academic, clinical, and economic importance of this group, this thesis began with a simple goal: to improve the current understanding LSPs in the PICU. To pursue this goal, LSPs are examined from multiple perspectives using a unique mix of sources and methods. Firstly, this thesis draws on valuable sources of unanalyzed information, in particular an original survey of PICU practitioners across Canada and an original dataset of a year of PICU admissions from a particular PICU. Secondly, this thesis uses unique methods, by applying survival analysis and logistic regression in tandem with a key informant survey. Finally, while previous literature has aimed to

identify LSPs' characteristics, this thesis brings a unique economic perspective by trying to understand their *impact*.

Using this unique mix of sources, methods, and perspectives, this thesis generates novel results to help further the understanding of LSPs in the PICU. While these results are discussed extensively in Chapter 4, two insights in particular are highlighted for their pertinence and originality.

Firstly, a framework for dichotomizing LSPs into "high-need" and "high-dependency" patients is established. High-need patients have long stays because they require long-term PICU treatment while high-dependency patients have long stays because there are not sufficient alternatives for them to receive care elsewhere. These two groups were defined based on the results of the survey. This proposed framework provides an important theoretical underpinning to clinical literature which has identified the need for a clear definition both of LSPs and the chronically critically ill and begins to bridge a gap in the discussion between these two related PICU populations (Marcus, Henderson & Boss, 2016; Nupen, 2015).

Secondly, there is a potential existence of congestion effects caused by LSPs. The empirical findings of this paper suggest that the stays of patients in this dataset were shorter on average when there were more LSPs in PICU. Using economic theory to analyze this finding suggests that this may be the existence of LSPs having a "congestion effect" which forces PICUs to ration the care they can make available to any individual patient.

Ultimately, this thesis argues that these findings have important research, clinical, policy, and economic implications. If some long stays result from a lack of sufficient care

alternatives as in the case of high-dependency patients, then researchers, clinicians, policy makers and economists should examine the costs and benefits of investing in new alternatives. Indeed, given that both complex chronic patients and LSPs share of the PICU population has been identified as growing, and since so many LSPs experience negative outcomes in the long-term, it is important that this group of high-dependency patients receives the care that is best suited to their needs (Edwards et al, 2013; Namachivayam et al, 2012). This point is underscored by the finding of potential congestion effects, which may increase the benefits of developing appropriate alternatives for the PICU and highlights the need for further researcher and economic analysis.

Since this thesis uses multiple methods to arrive at its conclusions, it will present the methods and results separately in the first three chapters, followed by a discussion of the interpretation and implications of the results in the final chapter. The first chapter describes the methods and presents the results of the survey. The second chapter outlines the methods and results of the empirical analysis of LSPs' characteristics. The third chapter examines the empirical methods and results of the analysis of how LSPs impact other patients. Finally, the fourth chapter discusses the interpretation of these results, and the implications of this interpretation on research and how LSPs are understood in the economic, clinical, and policy fields.

1 Chapter: Defining Long Stay Patients

This chapter focuses on a survey which elicited the perspectives of key stakeholders in PICUs across Canada regarding how to define LSPs in the PICU. This chapter will begin by reviewing existing definitions of LSPs in the clinical literature. Then. the process and methodology of the survey will be examined. Finally, the results of the survey will be presented. The implications and conclusions from the survey will be discussed in chapter 4.

1.1 Background

A small group of patients in the PICU stays long beyond the median length of stay (LOS) which is generally between 2 to 5 days (Marcin el al., 2001, Ruttimann & Pollack, 1996). The literature considers this group of LSPs to be particularly relevant because they consume a disproportionally large share of resources. Indeed, one study found that in one PICU only 4.4% of the patient population used 63% of the patient days, highlighting that a small group of patients, LSPs, can have important implications on how PICU's deliver care and manage resources (Naghib et al, 2010).

However, the justifications for defining LSPs used by different studies remain heterogeneous, for example:

- Consistency with adult studies (Pollack et al., 1987).
- Patients with LOS above the 95th percentile (Marcin et al., 2001)
- Three times the median length of stay (Naghib et al, 2010)
- Researcher judgement (van der Heide, 2004)

Such methods have resulted in the cut-off for LSPs ranging from 7 to 30 days. A recent literature review on LSPs in PICUs acknowledges that these heterogeneous

definitions are a barrier to understanding and applying current research in this area (Nupen, 2015). The review recommends that future research implements the approach used by *Weissman* to define LSPs in adult ICUs: namely applying multiple techniques and choosing the one best suited to a given data set (Weissman, 1997). These techniques include: inspecting histograms of frequency, five times the median LOS, two standard deviations above the mean, patients beyond the 75th percentile, and patients beyond the 95th percentile.

However, such an approach seems likely to make the definition of LSPs in research even more heterogeneous. Indeed, despite Weissman's development of these techniques for adult ICUs nearly 20 years ago, inconsistent definitions of LSPs in the adult ICU continue to be a commonly identified problem (Ettema et. al, 2010). Therefore, this thesis surveyed practitioners in the PICU to assess their perspectives on how best to define LSPs in the PICU. The survey assessed expert practitioners' perspectives on the importance of defining LSPs, the components of LSPs, the ideal characteristics of a definition of LSPs, and the methods for defining LSPs.

1.2 Survey Methods

The self-administered questionnaire was developed according to recently published recommendations for survey methodology (Burns et al, 2008). Relevant items for the questionnaire were identified through a literature review, all relevant items were considered, and then reduced to balance the need for information with respondent burden. The remaining items were appropriately formatted into a series of open and close-ended survey questions. The survey also collected basic demographic information to describe the participant population and to determine whether these factors influence participants'

survey responses. Finally, three individuals at the Children's Hospital of Eastern Ontario (CHEO) in comparable positions to the targeted survey population were identified to pilot the survey. The survey was revised according to the feedback of these pilot participants. The final survey contained open and close-ended questions and can be found in appendix A.

Fifteen tertiary care academic PICUs across Canada were identified to participate in the study, the PICU at Kingston General Hospital was excluded as a Level 2 PICU. Practical concerns meant the survey could only be administered in English, and as a result one centre, (Sherbrooke) was excluded due to linguistic barriers. Members of the thesis committee identified that it would be important to elicit the opinions of a medical director, nurse manager and hospital executive from each PICU. These three positions were considered key expert practitioners in the PICU, each potentially with a unique perspective regarding LSPs. A list with email contacts for the above personnel was generated using information from the internet, personal contacts at each site and through telephone contact with administrative assistants.

Ethics clearance was obtained from CHEO's research ethics board, with secondary clearance from Carleton's research ethics board. The survey was administered in English using the web-based software REDcap (Harris et al. 2009). After an initial invitation, participants who did not respond were sent email reminders after two and three week intervals. The medical directors who had not responded after this period were sent a final personalized message requesting their participation.

1.3 Survey Analysis

Quantitative questions

The survey consisted of both open and close-ended questions. The close-ended questions consisted of both multiple choice and ranking based questions. Multiple choice questions were reviewed and presented using frequencies and descriptive statistics accessed in the Microsoft Excel spreadsheet generated directly from the survey collection tool REDcap. The ranking based questions were similarly analyzed using frequencies and descriptive statistics in the statistical analysis software *Stata 14*. Statistically significant differences between ranked items were also analyzed using a Kruskal Wallis test followed by a series of Wilcoxon matched-pairs signed-ranks tests.

Kruskal-Wallis

This is a non-parametric test of whether two or more independent samples, in this case ranked items, originate from the same sample. It was considered ideal given the ordinal nature of the data. It tests the null hypothesis that the means of all relevant samples are equal by:

$$H = (N-1)\frac{\sum_{i=1}^{g} n_i(\bar{r}_i - \bar{r})^2}{\sum_{i=1}^{g}\sum_{j=1}^{n}(\bar{r}_{ij} - \bar{r})^2}$$

Where *n* represents a number of observations, *g* the number of groups, *r* represents a rank, a bar indicates an average, a subscript *i* represents a group and a subscript *j* represents an individual observation within a group. H approaches a chi-square distribution under the null hypothesis of no difference.

Wilcoxon matched pairs signed-ranks tests

This non-parametric test examines the null hypothesis that the means of two populations' ranks differ by:

$$W = \sum_{i=1}^{N}[sgn(x_{2,i} - x_{1,i})R_i]$$

Where relevant x's are paired rankings across the two groups, N is a reduced sample ordered from the smallest to largest absolute difference in pairs (excluding 0's) and R_i is the rank each pair receives in this order (or the average of ranks spanned for ties).

Under the null hypothesis, W follows a specific distribution with an expected value of 0. W can be assessed relative to a specified critical value to assess the null hypothesis.

Descriptive characteristics provide an easy to comprehend presentation of the survey results (and are included). However, they do not indicate where the differences in results are statistically significant, giving an important value added to the Kruskal-Wallis and Wilcoxon matched pairs signed-ranks tests. In other words, these tests are an objective way to assess the level of confidence that can be assigned to the fact that the observed results represent true differences in preferences, rather than random chance.

Additionally, these tests are preferred to similar tests such as the t-test or ANOVA because of their non-parametric nature, which means they do not assume the data follows a specific distribution. Firstly, the violation of the normal distribution assumption for parametric data is particularly concerning with small sample sizes, as is the case in this survey. Furthermore, this data is ordinal, meaning the relative distance between rankings is not known. For example, the difference between ranks 1 and 2 may not be the same as 3 and 4. Finally, while there is disagreement in the literature regarding whether Likert data should be treated using parametric on non-parametric tests, research suggests there may be no significant cost in terms of power or type 1 error to the use of either type test (de Winter & Dodou, 2010).

Qualitative questions

The qualitative questions were analyzed using the Framework method. This structured method for analyzing qualitative data outlined by *Ritchie and Spencer* is ideal for the exploratory nature this survey (Ritchie & Spencer, 2002). It allows for key results to arise from both the central research question and the specific nature of the responses. Additionally, the Framework method has been used in the literature to analyze qualitative data relating to LSPs in the PICU (Geoghegan, 2016). The five key steps of this method were implemented as follows:

- **Familiarization**: All the survey responses (both close and open-ended) were read through in full without taking notes. They were then re-read taking notes on key ideas and themes raised in each response.
- **Thematic Framework**: Key over-arching themes that were consistently raised by survey respondents were identified.
- **Indexing**: The responses were reviewed once again. Segments of responses were recorded under the key themes where appropriate.
- **Charting:** The responses recorded in the indexing phase were sorted comprehensively by theme into a table format.
- **Mapping and Interpretation:** Returning to the initial goals of the survey, this table was analyzed to observe its implications regarding a definition of LSPs.

1.4 Survey Results

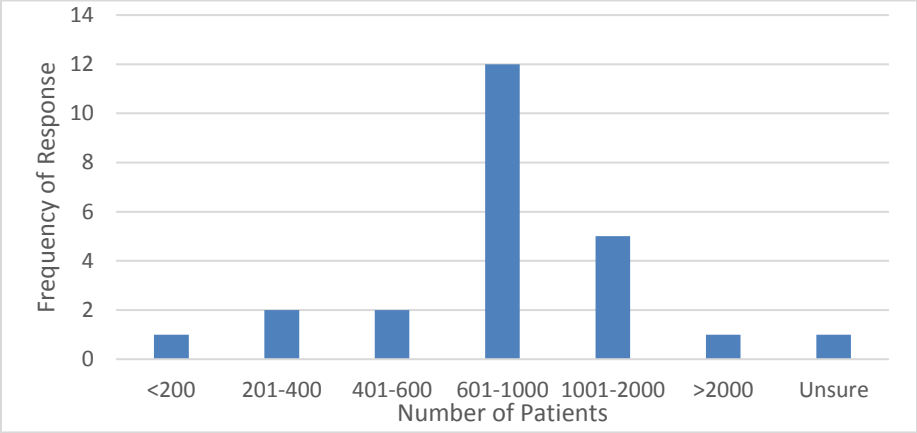
Forty-two potential experts in 14 centres were identified. However, contact information for two individuals could not be obtained resulting in 40 surveys being sent. The overall response rate was 70% (28/40) and at least one person from each centre

responded (with the exception of Centre hospitalier universitaire de Quebec). A full list of hospitals participating in the survey and the number of responses received from each is included in Appendix B.

Demographics

Of the 28 responses 12 (43%) were medical directors, 10 (36%) were nurse managers, and 6 (21%) were hospital executives. Of the PICUs, 11 (39%) had 5-10 beds, 10 had 10-20 beds (36%) and 7 (25%) had more than 20 beds. 20 respondents indicated that they had no separate area for LSPs, 4 indicated they had a specialized unit in a different location, 2 indicated designated beds in the PICU, 1 indicated specialized beds in the ward and 1 indicated future plans for a separate area. The reported number of patients per year in the PICUs is indicated in figure 1-1 below. Notably, there were some inconsistencies in PICU-specific variables across respondents in the same PICU.

Figure 1-1 Reported number of PICU patients per year



Importance of defining LSPs

21 respondents (78%) felt it was important to define LSPs while 3 (11%) felt it was not important and 3 were unsure*. Additionally, 24 (89%) of respondents felt it was important to include components other than LOS in a definition of LSPs, while 3 (11%)

** Percentages taken from total of 27 as one respondent did not respond to these two questions.*

did not*. Table 1.1 illustrates the close-ended responses regarding the opinions of respondents regarding specific reasons that it is important to define LSPs.

Table 1.1- Reasons for defining long stay patients

Reason	# of Respondents	Share of Positive Responses
Future PICU resource needs	18	86%
Determine alternate models of care	18	86%
Resource utilization	16	76%
Nursing staffing needs	14	67%
Compare PICU LOS data across units	12	57%

Method for defining LSPs

Respondents were asked to rank six factors regarding their relative preference for the definition of LSPs in the PICU and five methods of how to define LSPs. Each ranked item and its mean, mode, and median ranking can be found in tables 1.2 and 1.3. Lower numbers indicated a higher preference.

Table 1.2- Rankings for preferred methods

Method	Mean	Median	Mode
Percentile	1.92	2	1
Pre-defined Cut-off	2.58	2	2
Multiple of the Average	3.24	3	3
Share of Resources	3.31	4	4
Subjective	3.81	5	5

Table 1.3- Rankings for preferred factors

Factor	Mean	Median	Mode
Consistent	2.82	3	1
Useful	2.93	3	2
Easy to Use	3.18	3	2
Flexible	3.62	4	4
Precise	3.89	4	5
Exhaustive	4.04	5	6

There was a significant difference in the frequency of the methods preferred for defining LSPs as well as for the factors felt to be important by the respondents. For the methods, a Kruskal-Wallis test found chi-squared value of 21.206 and a p-value of 0.0002. For the factors, the same test found a chi-squared value of 10.714 and a p-value of 0.05.

The results of the Kruskal-Wallis test justified post-hoc analysis. Each item was compared using a Wilcoxon matched pairs signed-rank test. For the methods, the *percentile* was found to be significantly higher than all other options except *pre-defined cut-off* at a <1% level. Additionally, *pre-defined cut-off* outranked *subjective* at 5%, and *share of resources* at 10%. For the factors, *useful* and *consistent* both outranked *precise* at the 5% level. At the 10% level *useful* outranked *flexible*, *consistent* outranked *exhaustive* and *easy to use* outranked *precise*.

Qualitative responses

The key themes raised and the number of responses that identified these themes are presented in table 1.4:

Table 1.4- Categorized qualitative responses (frequencies)

Theme	Number of responses
Factors to consider in a definition of LSPs besides LOS	
Patient condition (diagnosis, complexity, stability)	14
Acuity/resource use	9
Technology requirement/dependence	8
Available alternatives to PICU	4
Acute nature of patient	4
Family situation/support	4
Recurrent admissions	2
Importance of defining LSPs (other responses)	
Staffing needs/resource management	6
Pathway of care/alternative care/other places for care	5

Not important to define	3
Comments on methods	
Comparability/objectivity is important	6
Definition should be practical/easy to use	3
Specific hospital's circumstances are important	2
Must account for many important variables	2

Additionally, specific quotes relevant to the research question were retained and will be referred to during the analysis in Chapter 4 where appropriate. A table of these reserved quotes is included in Appendix C.

Cross Sectional Analysis

Responses were analyzed according to respondents' characteristics and their other responses for patterns. The relatively small sample size and mix of quantitative and qualitative information made it difficult to test for statistically significant differences between groups. However, some descriptive statistics that were considered of interest are listed below.

For the rankings of methods, 6/12 (50%) of respondents who ranked *percentile* first ranked *predefined cut-off* second, while 4/7 (57%) who ranked *predefined cut-off* first ranked *percentile* second, indicating these two responses are positively associated. 4/6 (67%) of those ranking *predefined cut-off* at number 1 ranked *subjective* at number 5, while both individuals ranking *subjective* at number one ranked *predefined cut-off* last, indicating these responses were negatively associated. 8/12 (67%) of those who ranked *percentile* first ranked *subjective* last, while *percentile* was not ranked low by those who thought positively of the *subjective* method. No similar trends were observed for the factors.

Regarding the qualitative responses, 7 of the 8 respondents who identified *technology dependence* as an important factor were medical directors, indicating this issue was raised by 58% of medical directors. Of the 6 who thought the definition should be used to decide to make *staffing/resource decisions*, 4 were medical directors. All three respondents who emphasized the *need for a practical/easy to use definition* were medical directors. 6 (60%) of nurse managers identified the importance of including *patient condition* in a definition of LSPs. 3 (50%) of hospital executives emphasized the importance of including *acuity* in a definition of LSPs.

2 Chapter: Characteristics of Long Stay Patients

This chapter examines the characteristics of LSPs and LOS in the PICU using four empirical methods on a dataset of 523 PICU stays. It uses an (i) accelerated failure time (AFT) regression to determine which patient characteristics are associated with longer LOS, and applies a (ii) logistic regression to determine the patient characteristics associated with LSPs. Finally, it complements the AFT regression with (iii) quantile and (iv) Laplace regressions to identify the effect of different variables at different stages in the distribution of the outcome length of stay.

The chapter begins by providing necessary background for this paper, noting important points from the literature regarding the analysis of LOS and LSPs. The next section examines the methods used in this paper including a discussion of their advantages, disadvantages and limits. Finally, the results of this analysis will be presented. Note, that the analysis and discussion of the results will be in chapter 4.

2.1 Background

PICU Length of Stay

While LSPs have been identified as the key interest of this thesis, this concept is closely tied to that of LOS. Additionally, as an interval variable, LOS contains more detailed information than a binary outcome such as LSP. Hence, this thesis will examine both LOS and LSP as outcomes in the PICU.

Survival analysis will be used to analyze LOS as it addresses the empirical problems where the outcome variable of interest is the time until an event occurs (Kleinbaum & Klein, 2012). In the case of LOS, discharge from the PICU is the event of interest. Survival analysis effectively accounts for LOS data which is highly right-

skewed, which is especially important given the emphasis this thesis places on LSPs (Cleves et al, 2010). For a broader review of different methods used in the literature to analyze LOS, see *Castillo 2012*.

The application of survival regression to this kind of data is supported by previous studies which analyzed LOS in the PICU. For example, in a large and commonly cited study of PICU LOS in the United States, *Ruttiman and Pollack* analyzed 5415 admissions from 16 PICUs using the same method of survival analysis applied to this thesis: an accelerated failure time model parameterized with a log-logistic distribution. They found that Pediatric Risk of Mortality Score (PRISM) score, operative status, inpatient/outpatient status, previous PICU admission, first day mechanical ventilation and 10 diagnostic groups were significant patient-related predictors of PICU LOS.

Some articles that have applied survival analysis to LOS in the adult intensive care unit (ICU) put a more explicit emphasis on discussing the methods they use. This literature primarily focuses on how to treat mortality in a survival regression: through censoring or as a competing risk (Barilli et al., 2012, De Cocker et al, 2011). Together with recent work examining LOS outside an ICU setting, the growing consensus appears to be that it is conceptually correct to treat this group as a competing risk (Brock et al, 2011; Chaou et al, 2016).

PICU Long Stay Patients

A strand of clinical literature tries to better understand the differences in the characteristics and outcomes of patients who stay longer in the PICU. Notably, no definitive set of characteristics of LSPs has been established in this literature, and certainly not in Canadian PICUs. However, *Marcin et al*'s study, with a sample size of

11,165 admissions to 32 ICUs, is one of the largest and most cited sources for characteristics of LSPs in the PICU and suggests a set of important characteristics. The authors apply a logistic regression and find similar factors to those identified by *Ruttiman and Pollack* for LOS, summarized in the following table:

Table 2.1- Marcin et. al. results

Variable	Odds Ratio (p-value)
Age less than one year	1.77 (0.00)
Postoperative*	0.69 (0.004)
Previous ICU admission*	2.18 (0.00)
Emergency admission*	1.63 (0.00)
CPR before admission	0.59 (0.032)
Admit from another ICU*	2.28 (0.02)
Never discharged from hospital*	3.09 (0.006)
Chronic TPN	2.23 (0.00)
Chronic tracheostomy	2.27 (0.02)
Ventilator*	4.59 (0.00)
Intracranial catheter	2.78 (0.00)
PRISM score from 10-33*	2.99 (0.00)

**Similar to a factor found in Ruttiman and Pollack*

Differences in outcomes of LSPs compared to other patients have also been identified. LSPs suffer more complications (van der Heide, Hassing & Gemke, 2004) and unfavorable outcomes (Namachivayam et al., 2012), and differ on measures of morbidity, mortality, and resource consumption (Gonzalez-Cortes et al, 2011). While this is not being directly examined by this thesis, it emphasizes the importance of studying LSPs in different contexts.

2.2 Methods

Data

This is a secondary analysis of a prospectively collected dataset of 523 distinct admissions to CHEO's PICU. CHEO is a tertiary care academic pediatric centre located in Ottawa, Ontario, Canada with more than 6,600 admissions, 7,700 surgeries and

171,000 clinic visits each year. CHEO services a catchment area which includes ~1.5 million people and encompasses Eastern Ontario, Western Quebec and Nunavut. The data was collected from February 1st, 2015 to January 31st, 2016.

Data collected included patient level and unit level variables. Patient level variables were hospital admission time, PICU admission time, PICU discharge time, age, diagnosis, previous hospital admissions, illness severity scores (including PRISM score) and treatments received (ie. mechanical ventilation). Unit level data included daily nursing staffing ratios, refused admissions and cancelled surgeries.

Defining LSPs

Sensitivity analysis was used to identify the 92nd percentile to cut off a definition of LSP. This method and the criteria are based on are the results presented in chapter 1 and analyzed in chapter 4. Using the data summarized above, LSP was used as the sole predictor in logistic regressions on four outcomes: beyond the 95th percentile of time on a peripherally inserted central catheter, beyond the 90th percentile of time on mechanical ventilation, more than 60% of a stay with an arterial line inserted and more than 60% of a stay with a central venous line inserted. The justification for the use of these four outcomes is provided in chapter 4. Specifically, the following four logistic regressions were each estimated 10 separate times, with 10 different cut-offs for LSP:

$$\Pr[> 95th\ peripherally\ inserted\ catheter_i = 1]\ |LSP_i| = \frac{\exp(\boldsymbol{LSP}'\beta)}{1 + \exp(\boldsymbol{LSP}'\beta)}$$

$$\Pr[> 90th\ mechanical\ ventilation_i = 1]\ |LSP_i| = \frac{\exp(\boldsymbol{LSP}'\beta)}{1 + \exp(\boldsymbol{LSP}'\beta)}$$

$$\Pr[> 60\%\ arterial\ line_i = 1]\ |LSP_i| = \frac{\exp(\boldsymbol{LSP}'\beta)}{1 + \exp(\boldsymbol{LSP}'\beta)}$$

$$\Pr[> 60\%\ central\ venous\ line_i = 1]\ |LSP_i| = \frac{\exp(\boldsymbol{LSP}'\beta)}{1 + \exp(\boldsymbol{LSP}'\beta)}$$

The area under the receiver operator curve (ROC) was used to assess predictive power for each of the 10 different cut-offs for LSP. The ROC was used as it considers the rate of both the true and false positives created by different cut-offs. The results are presented in table 2.2.

Survival Analysis

Description

The effect of patient's covariates on their LOS will be assessed using an accelerated failure time (AFT) model parameterized with a log-logistic distribution. This model assumes that the baseline survival function for all patients follows a log-logistic distribution, and individual patients' stays vary based on the direct effect of their covariates on time in the PICU represented by the parameter θ below:

$$S(t) = \frac{1}{[(1 + (\theta t)^p)]}$$

The advantages and disadvantages of this model for the data under consideration are discussed below relative to a popular alternative, the semi-parametric Cox proportional hazards (PH) model. An in-depth treatment of survival analysis, the semi-parametric Cox PH model and the parametric AFT model is given in Appendix D.

Model Selection

For this empirical problem, the parametric AFT model is generally preferred to the semi-parametric Cox model if the appropriate assumptions hold. Although it is not a consensus (Moran et al, 2008), studies comparing Cox to parametric AFT models have noted that in cases where the PH assumption fails a parametric AFT model may be

preferred (Knaus el al, 1993, Kay & Kinnersley, 2002, Kwong & Hutton, 2003). Both graphical and quantitative tests indicate that the PH assumption fails in the case of this data when modelling the effect of the relevant covariates on LOS. In particular, a test based on Schoenfeld residuals (described in Cleves et. al., 2010) under the null-hypothesis that the PH assumption holds produces a chi-squared value of 36.92 with 13 degrees of freedom and a p-value of 0.0004, providing evidence that the PH assumption is violated.

Additionally, the AFT model has been shown to be less susceptible to omitted covariates/heterogeneity, of particular importance in this cross-sectional observational dataset (Kalbfleish & Struthers, 1986; Keiding et. al, 1997). Finally, the goal of this chapter is to identify statistically significant associations which can be used to develop a predictive model of patients' discharge (failure) times, and "with Cox regression, little attention is paid to the actual failure times, and predictions of these failure times are seldom desired" (Cleves et. al., 2010).

While the AFT model may be generally preferred in this case, the key question remains if it is appropriate to assume that its survivor function and underlying risk process (the hazard) follows the assumed parameterization. The hazard functions for two common parameterizations, the Weibull and the log-logistic are included in Appendix E using the variables identified below. Notably, while the AFT model is not concerned with the direct effect of different factors on the hazard, this is the risk process underlying survival time, and so it is still relevant to scrutinize what this risk process is assumed to be.

The Weibull shows that the risk of discharge increases over time, while the log-logistic shows a sharp increase, followed by a decreasing risk of discharge over time. Unfortunately, since the underlying risk process of each patient is not observed, the choice of a parameterization and confidence in that choice is a fundamentally theoretical assertion. Given the long right tail in the outcome (LOS), this thesis asserts that it is most appropriate to assume that the underlying risk process decreases over time, and hence the log-logistic parametrization. Indeed, this has argued by past work (Ruttimann & Pollack, 1996), and is further supported by an assessment of the Akaike Information Criterion (see Cleves et. al., 2010), and the Cox-Snell residual test for model fit (see figure 2.1).

However, it is important to remain skeptical of this assumption. With limited theoretical basis for deciding on a baseline hazard rate, this thesis will proceed with the log-logistic model as the best fit for the data, and hence the best approach to moving towards a model that is predicative of LOS. However, it proceeds with the caveat that the assumed parametrization is questionable. To try and remedy some of this uncertainty, the model is supplemented with quantile and Laplace regressions.

Quantile Regression

The modelling of LOS is supplemented with quantile regression. As identified by the discussion above, there are reasons to be concerned that the effect of the covariates on LOS may vary along the LOS distribution. For example, short stay patients' LOS may significantly vary by their PRISM score, while this is not the case for LSPs.

Quantile regression models the effect of covariates on a dependent variable by minimizing the following objective function over β_q:

$$Q_N(\beta_q) = \sum_{i:y_i \geq \boldsymbol{x}'_i\beta}^{N} q\left|y_i - \boldsymbol{x}'_i\beta_q\right| + \sum_{i:y_i < x_i\beta}^{N} (1-q)|y_i - \boldsymbol{x}'_i\beta_q|$$

This allows the researcher to examine how the covariates impact LOS for patients with different LOS. For example, if the 5th quantile (q=0.05) is selected, the variation in the LOS and x's of patients with shorter stays is given far more weight in determining the parameter of interest (β). The opposite is true at q=0.95, while q=0.5 is comparable to standard regression examined at the median rather than the mean.

Laplace Regression

Additionally, the effect of covariates at different levels of LOS can be assessed within the survival analysis framework using Laplace regression. This examines the absolute differences in survival time at a particular level of the survival function. For example, if for group one $S_1(10)$=0.9 while for group two $S_2(20)$=0.9, the Laplace regression would compare the absolute difference between 10 and 20 to find that the effect of being in group 2 is 10 units of time. Estimation is carried out by maximizing a non-differentiable likelihood function. Details regarding the estimation and a user-friendly command on Stata are provided by *Bottai & Zhang* and *Bottai & Orsini* (Bottai & Zhang, 2010; Bottai & Orsini, 2013).

Competing Risks

Finally, this thesis acknowledges the growing consensus in the literature that it is correct to treat mortality as a competing risk. However, it is notable that the dataset used for this thesis observes only 12 out 523 cases that ended in death. For this dataset, treating death as censored relative to a competing risk causes only slight changes in the coefficients and standard errors and no changes in the conclusions of the model.

Additionally, it is notable that treating deceased patients as censored simplifies the analysis for practical purposes. Therefore, while it is likely conceptually correct to use a competing risks framework, death is treated as censoring for practical purposes since this simplification is not seen to significantly impact the results.

Logistic Regression

This model is used to predict a patient's probability of being a LSP where the outcome is a binary variable that takes on a value of 1 if the patient is an LSP, and 0 otherwise. In the case of a binary outcome variable an OLS regression ignores the discreteness of the dependent variable and does not constrain predicted probabilities to be between 0 and 1 (Cameron & Trivedi, 2005). To contrast, a logit model specifies:

$$p_i = \Pr[y_i = 1]\,|x_i| = \frac{\exp(\boldsymbol{x}'\beta)}{1 + \exp(\boldsymbol{x}'\beta)}$$

Where the coefficients are estimated through maximum likelihood estimation. While β shows the marginal effect of a covariate on the conditional probability of the outcome being one, results are reported in terms of odds ratios:

$$p = \frac{\exp(\boldsymbol{x}'\beta)}{1 + \exp(\boldsymbol{x}'\beta)}$$

$$\frac{p}{1-p} = \exp(\boldsymbol{x}'\beta)$$

$$\ln\left(\frac{p}{1-p}\right) = \boldsymbol{x}'\beta$$

Here p/(1-p) is the odds ratio, and measures the probability that y=1 relative to the probability y=0, or in this case the probability that a patient is an LSP *relative* to the probability that they are not. Hence, the logit model's slope parameter can be interpreted as a semi-elasticity that increases the odds ratio by a multiple of β. Unlike an OLS

regression coefficient, this acknowledges the discrete nature of the outcome and constrains the predicted probability of the outcome occurring to be between 0 and 1. Notably, the largest study examined for this paper that use LSPs as a dependent variable applies logistic regression and reports the odds ratios (Marcin et. al. 2001).

Model Fit

Finally, the fit of both the survival regression and the logistic regression were assessed using the following methods:

Cox-Snell Residuals

A Cox-Snell residual is defined as:

$$CSr_j = \widehat{H}_0(t_j)\exp(\boldsymbol{x_j}\widehat{\beta_x})$$

Where $\widehat{H}_0$ and $\widehat{\beta_x}$ are obtained from the model. If the data fits the survival regression well, the Cox-Snell residuals should have a standard exponential distribution (Cleves et al., 2010). If the residuals met this distribution they would have a constant hazard function at 1 and a cumulative hazard rate that is a straight line. Therefore, the fit of the log-logistic model is assessed by plotting the Nelson-Aalen cumulative hazard of the Cox-Snell residuals against the residuals themselves as a 45° reference line. The results are provided in figure 2.1 in the results section.

Receiver Operator Curve

The predictive ability of the logit model was assessed using the ROC (Zou et al, 2007). In models that distinguish between two potential outcomes, in this case being an LSP or not, a cut point is defined to sort observations into one group or another based on their covariates. The ROC varies these cut points and plots the false positive rate against the true positive rate (see figure 2.2). In this case, a model with no predictive power

would be a straight line with a slope of one, while a perfectly predictive model would plot a vertical line tracking the y-axis and a horizontal line at a 100% true positive rate. The predictive power of the model can be assessed by examining the area under the ROC, as this indicates where the ROC falls between the two extremes of perfect and zero predictive power. An area of 1 is perfect, an area of 0.5 has no predictive power.

The predictive power of the logit model for this thesis was assessed by splitting the sample in half into testing and verification samples. This is to simulate the application of the model to data other than that on which it was estimated (hence better evaluating predictive power). The sample was randomly split 50 times for more robust results. The results are provided in the results section.

Selecting Variables

All variables in this dataset were considered for their potential effect on LOS. Each variable's relationship to the dependent variable was tested by including it in the relevant regression framework alone, and in alternate functional forms/combinations with other variables where appropriate. Significant variables indicated by a p-value below 0.05 were retained for further analysis. Additionally, variables whose significance suggested no utility for a predictive model for practical or theoretical reasons were omitted.

When included with all other variables as controls, each covariate was reassessed for its significance by scrutinizing the variable in different combinations with other variables. The decision to include different combinations of variables was based on sensitivity analysis which compared the Akaike Information Criterion for the survival regression and the ROC for the logistic regression. A list of variables omitted from the model is included in Appendix F along with an indication of *why* they were omitted.

This process was followed for both the survival regression and the logistic regression. However, the quantile and Laplace regressions used the same covariates as the survival regression. This is because these models are used as a tool to assess the average effects produced by the survival regression, rather than to draw new conclusions regarding factors potentially associated with LOS.

Included Variables

A full list of the included variables can be seen in tables 2.3 and 2.4. The presence of various treatments were recorded for all patients, these variables took on a value of 1 if present during the patient's stay, 0 if not. Of these, the significant treatments were: arterial lines, peripherally inserted intravenous catheters, mechanical ventilation, non-invasive ventilation, nitric oxide, being in isolation during admission, and ECMO. Age<1 was assigned a value of 1 for age < 1 year and 0 if age $\geq$ 1 year. Re-admit from ward was given a value of 1 if the patient was re-admitted to the PICU after being discharged to the ward from the PICU, 0 otherwise. Operating room and ward admissions were given a value of 1. Medical cardiac patients were given a value of 1 if this characterized the patients' "admit type".

PRISM is the patient's Pediatric Risk of Mortality (PRISM III) score and is based on physiologic, therapeutic and demographic variables (Pollack, Patel & Ruttimann, 1996). PRISM represents the patient's risk of mortality but is often used as a surrogate for illness severity. Studies assessing the effect of PRISM on LOS/LSP examine how the mean LOS changes with PRISM to assess the best way to include it in the model (Marcin et. al. 2001, Ruttimann & Pollack 1996). Using this method, no clear pattern emerged beyond a simple linear relationship with LOS and so the PRISM score was included

directly with LOS as an outcome. The same method found the binary variable PRISM>11 (beyond the 90th percentile of PRISM scores in the sample) was best for LSP.

2.3 Results

Descriptive Statistics

The median LOS in the sample is 1.87 days (IQR: 5.7-0.9; range: 0.1-85.5) and the mean is 4.61 ± 7.6 days. The total number of patient days is 2413. Half (1207) of the total bed days were used by only 12% of patients. The mean age is 6 ± 6 years old and the median age is 3 (IQR: 12.1-0.6; range: 0-20) years old.

116 of the 523 admissions, were re-admissions of 47 patients previously observed in the dataset. Of these, 2 patients have 5 stays, 4 have 4 stays, 8 have 3 stays and 33 have 2 days. Twelve patients were deceased, 10 during the study period and two following.

Definition

Below are the results of the sensitivity analysis used to identify the specific percentile cutoff used to define LSPs.

Table 2.2- Predictive power at different percentiles

	50	**65**	**75**	**80**	**85**	**87**	**90**	**92**	**93**	**95**
Top 10% of time on mechanical ventilation	0.74	0.82	0.88	0.90	0.93	0.94	0.96	0.97	0.91	0.84
Top 5% of time on peripherally inserted central catheter	0.61	0.68	0.74	0.76	0.78	0.80	0.81	0.82	0.83	0.84
Over 60% of stay with arterially line inserted	0.54	0.53	0.51	0.51	0.50*	0.50*	0.50*	0.50*	0.50*	0.51*
Over 60% of stay with	0.57	0.58	0.55	0.53	0.51	0.51	0.50	0.51	0.51	0.50

central line inserted										

**predicts a negative relationship*

The 92nd percentile was selected because it was most associated with mechanical ventilation, close to the most associated with peripherally inserted central catheter, and unassociated with the last two variables. These results are discussed in chapter 4.

Model Results

Below are the set of variables identified as associated with the outcome with LOS.

Table 2.3- AFT regression on LOS

Log likelihood: -570.53
Number of observations: 523

Variable	Coefficient	Standard Error	p-value	95% Confidence Interval
Peripherally insterted central catheter	0.85	0.09	0.000	0.66-1.04
Arterial lines	0.44	0.08	0.000	0.28-0.61
Mechanical ventilation	0.56	0.08	0.000	0.41-0.71
Non-invasive ventilation	0.67	0.08	0.000	0.51-0.83
Nitric Oxide	0.48	0.19	0.009	0.12-0.84
Isolated during stay	0.36	0.08	0.000	0.20-0.51
ECMO	1.09	0.49	0.027	0.13-2.06
Operating Room	-0.24	0.08	0.004	-0.40-(-0.08)
Ward	0.43	0.12	0.000	0.20-0.66
Ward Re-Admit	0.62	0.12	0.00	0.39-0.85
PRISM	0.03	0.01	0.001	0.01-0.04
Age<1	0.18	0.07	0.015	0.04-0.32
Constant	-0.29	0.06	0.00	-0.42-(-0.17)

*Significant at: ***<1%, **<5%, *<10%*

12 variables were found to be associated with LOS. Of these, those with the largest coefficients are the interventions the patient received. Other factors include where the patient is admitted from, the patients' age, and PRISM score. These results are discussed in chapter 4.

Below are the set of variables identified as associated with LSP.

Table 2.4 Logit model on LSP

Pseudo R^2: 0.3631
Number of observations: 523 (42, LSP=1; 481, LSP=0)

Variable	Odds Ratio	Standard Error	p-value	95% Confidence Interval
Peripherally insterted central catheter	9.00	3.77	0.000	3.96-20.43
Mechanical ventilation	5.02	2.61	0.002	1.81-13.90
Non-invasive ventilation	2.82	1.16	0.011	1.26-6.30
Isolated during stay	3.19	1.33	0.005	1.41-7.22
Ward Re-admit	2.16	1.11	0.134	0.79-5.90
Medical Cardiac	12.53	10.99	0.004	2.25-69.88
Age<1	1.70	0.70	0.195	0.76-3.81
PRISM>11	1.82	1.01	0.278	0.62-5.39
Constant	0.01	0.002	0.000	0.001-0.009

*Significant at: ***<1%, **<5%, *<10%*

5 variables were found to be significantly associated with LSP. 4 were interventions that the patients received. The other was a patient diagnosis type. Additionally, the patient's age, PRISM and where they were admitted from added predictive power. These results are discussed in chapter 4.

Below are the results of the quantile and Laplace regressions.

Table 2.5- Quantile and Laplace regressions

ln(LOS)	5	25	50	75	95
Quantile: Coefficient (Bootstap SE)					
Peripherally insterted central catheter	0.59*** (0.19)	0.84*** (0.17)	0.93*** (0.13)	0.89*** (0.14)	1.32*** (0.25)

Arterial lines	0.60*** (0.17)	0.59*** (0.12)	0.34*** (0.13)	0.49*** (0.18)	0.19 (0.18)
Mechanical ventilation	0.12 (0.18)	0.39*** (0.10)	0.61*** (0.08)	0.65*** (0.14)	0.67*** (0.17)
Non-invasive ventilation	0.90*** (0.18)	0.75*** (0.11)	0.69*** (0.15)	0.72*** (0.00)	0.60*** (0.21)
Nitric Oxide	0.21 (0.25)	0.18 (0.37)	0.34 (0.25)	-0.02 (0.23)	-0.56** (0.24)
Isolated during stay	0.28* (0.16)	0.31** (0.13)	0.31** (0.13)	0.28** (0.13)	0.59*** (0.17)
ECMO	-0.48 (0.80)	-0.01 (0.81)	0.40 (0.62)	0.19 (0.44)	-0.21 (0.35)
Operating Room	-0.12 (0.19)	-0.22* (0.12)	-0.20 (0.13)	-0.37*** (0.12)	-0.02 (0.14)
Ward	-0.01 (0.29)	0.40* (0.24)	0.49*** (0.16)	0.39** (0.16)	0.67 (0.43)
Ward Re-Admit	0.54 (0.34)	0.60*** (0.21)	0.57*** (0.18)	0.58*** (0.18)	0.53** (0.26)
PRISM	0.04*** (0.01)	0.02* (0.01)	0.02 (0.01)	0.02 (0.02)	0.02 (0.01)
Age<1	0.09 (0.18)	0.13 (0.09)	0.14 (0.10)	0.28** (0.11)	0.29 (0.19)
Constant	-1.32*** (0.13)	-0.71*** (0.07)	-0.26*** (0.07)	0.22** (0.11)	0.84*** (0.17)
LOS	**5**	**25**	**50**	**75**	**95**
Laplace: Coefficient (Robust SE)					
Peripherally insterted central catheter	0.72** (0.33)	3.63*** (0.75)	5.33*** (0.67)	6.62*** (0.85)	18.76*** (3.16)
Arterial lines	0.46*** (0.14)	0.49** (0.21)	0.54** (0.26)	1.84*** (0.52)	0.74 (0.60)
Mechanical ventilation	0.20 (0.12)	0.48** (0.19)	1.04*** (0.25)	1.94*** (0.55)	3.15*** (1.14)
Non-invasive ventilation	0.76*** (0.22)	0.83*** (0.28)	1.85*** (0.40)	2.98*** (0.53)	7.17** (3.61)
Nitric Oxide	0.56 (1.97)	3.71*** (1.25)	3.76** (1.87)	4.91*** (1.74)	-2.11** (0.98)
Isolated during stay	0.26* (0.15)	0.36 (0.23)	0.71** (0.28)	0.95*** (0.34)	2.40 (1.86)
ECMO	4.88** (2.12)	4.09** (1.61)	3.93*** (0.90)	4.78 (6.82)	9.06 (8.82)
Operating Room	-0.15 (0.11)	-0.17 (0.18)	-0.23 (0.23)	-0.13 (0.35)	-0.07 (0.31)
Ward	0.15 (0.26)	0.45 (0.45)	0.70 (0.48)	1.50** (0.62)	4.71 (4.57)

Ward Re-Admit	0.70** (0.30)	0.88* (0.48)	1.65** (0.74)	2.47*** (0.91)	11.53*** (3.04)
Age<1	0.26** (0.12)	0.14 (0.21)	0.06 (0.25)	0.67* (0.40)	1.65 (1.97)
PRISM	0.03** (0.02)	0.04 (0.03)	0.06* (0.03)	0.09** (0.05)	0.17 (0.13)
Constant	-0.07 (0.14)	0.35 (0.22)	0.51* (0.28)	0.70 (0.44)	1.67 (1.54)

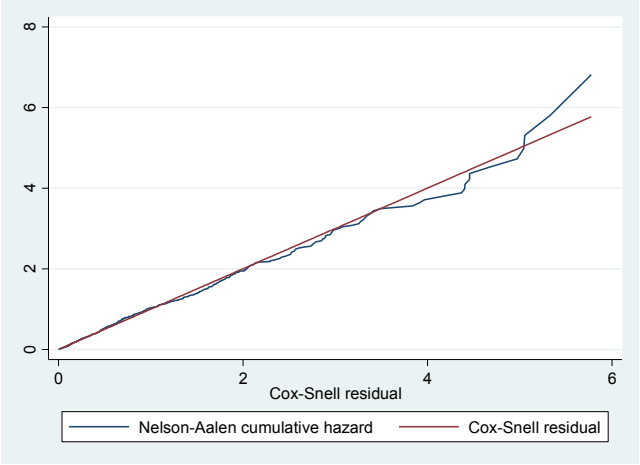
*Significant at: ***<1%, **<5%, *<10%*
A graphical representation of these results in provide in Appendix G

These results illustrate how the effect of the variables in table 2.3 vary according to the percentile of LOS at which they are assessed. The nature of this variation is discussed in chapter 4.

Model Fit

The Cox Snell residual test presented below assess the fit of the predictions made by the AFT regression to the data.

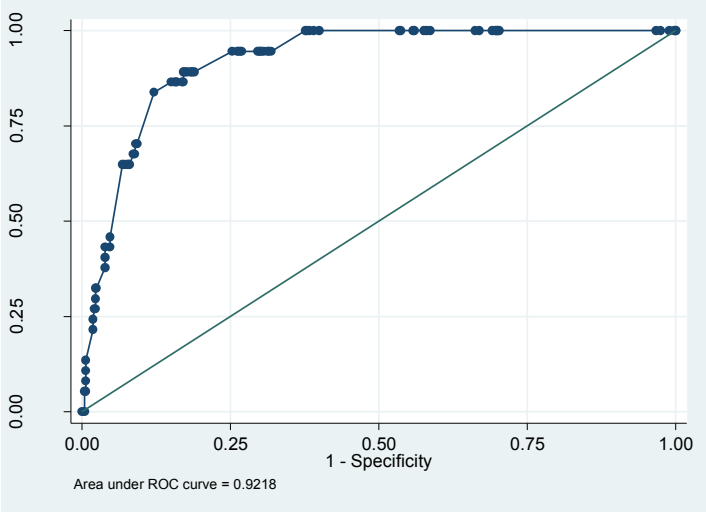
Figure 2-1- Plot of cumulative hazard function of Cox Snell residuals of the AFT



The extent to which the blue hazard estimate mirrors the red reference line reflects the fit of the model. The degree of fit is discussed in chapter 4.

The average area under the ROC for these 50 splits was 0.92 for the testing sample and 0.89 for the verification sample. The ROC for both samples is presented below. These results are discussed in chapter 4.

Figure 2-2- Receiver operator curve for the full sample



3 Chapter: The Impact of Long Stay Patients

The primary goal of this chapter is to examines the impact of LSPs. Previous studies note that the high share of hospital days consumed by this small population indicate that they consume a high share of hospital resources (Naghib et al, 2010). Economic reasoning suggests this analysis can be extended, as a limited number of PICU beds and staff mean that hospitals are forced to make decisions regarding the allocation of scarce resources. Through this lens, PICU care is to some degree a rival good, indicating the large number of PICU days consumed by LSPs may restrict the access of others to this good.

In this way, one *impact* of LSPs might have is to reduce the LOS of other patients. In particular, since inputs such as PICU beds are fixed in the short run, hospitals may be under more pressure to ration PICU days when there are a relatively higher number of LSPs. Hence, this chapter aims to investigate the relationship between the number of LSPs in the PICU and a patients' LOS. A review of the literature found no other work trying to address this question. Although the novelty of this analysis makes it original, it is also preliminary, as it has little precedent to support it.

This chapter uses survival analysis to try and identify the relationship between the presence of LSPs in the PICU and other patients' LOS, while controlling for identified confounding factors. Additionally, patients with multiple stays during the study period are exploited as a robustness check for the presence of patient-invariant bias.

This chapter draws heavily on the same data and methods as Chapter 2. The discussion of the data and survival analysis are not repeated here. Instead this chapter

reviews only the additional points regarding data and methods that are new to this analysis. This will be followed by a presentation of the results. These results will be discussed in the following chapter.

3.1 Methods

Data

For an overview of the dataset used in this chapter, see chapter 2. The primary distinction and innovation of this data relative to that used in chapter 2 is the creation of a new variable using the information underlying the dataset. Specifically, by using the admit and discharge date of each patient, it was possible to identify which patients had overlapping stays. Using this, for each patient two variables were created: the number of total overlapping days between a patient and all other patients, and the number overlapping days with other LSPs. From here the average number of other patients and LSPs per day was generated for each patient:

$$Other\_Patients\_Per\_Day_i = \frac{Total\ Time\ Overlapping\ with\ Other\ Patients_i}{Length\ of\ Stay_i}$$

$$Other\_LSPs\_Per\_Day_i = \frac{Total\ Time\ Overlapping\ with\ Other\ LSPs_i}{Length\ of\ Stay_i}$$

Taking the ratio of these two variables creates the ratio of LSPs to other patients over the patient's stay.

$$LSP\_Ratio_i = \frac{Other\_LSPs\_Per\_Day_i}{Other\_Patients\_Per\_Day_i}$$

Survival Analysis

Much like chapter 2, the outcome of interest for this chapter is a patient's LOS. This chapter uses the same methods of survival analysis and quantile regression outlined in the methods section of Chapter 2.

However, unlike in chapter 2, the assumption of a log-logistic survivor function will be relaxed. In this chapter, the goal is to investigate the relationship between a specific variable and its outcome. Therefore, it may be appropriate to be more skeptical of the assumption that the survivor function and its underlying risk process follow an assumed parametrization. To try and relax this, an AFT with both a log-logistic and Weibull distribution will be used, along with the semi-parametric Cox PH. Additionally, a quantile and Laplace regression will be used (as described in Chapter 2).

Robustness Check: Test for Patient-Invariant Bias

If a relationship exists between LOS and the number of LSPs in the PICU, one would expect the LOS of a single patient with multiple stays to follow the same relationship. Therefore, this analysis takes advantage of the fact that 116 of the observations come from 47 patients, by running a fixed effects regression and using a Hausman test to compare it to a random effects alternative. Such a test could identify the existence of effects of unobservable patient characteristics which may be biasing the results.

The time between patients' stays varies for each patient. Different patients have different numbers of stays: 2 patients have 5 stays, 4 have 4 stays, 8 have 3 stays and 33 have 2 stays. This segment of patients is not necessarily representative of the entire population. For example, the mean LOS for the panel was 6.64 ± 10.6 days, versus a mean of 4.03 ± 6.45 days for those stays not included in the panel.

For the fixed effects regression used for this robustness check, each observed covariate and outcome, the mean value for that individual and the mean from the sample is subtracted. The subtraction of an individuals' mean allows for the elimination of

individual specific factors biasing the results. Subtracting the population mean allows for the estimation of an intercept.

$$y_{it} - \overline{y_i} - \overline{\overline{y}} = \propto \ + (x_{it} - \overline{x_i} - \overline{\overline{x}})'\beta + (\varepsilon_{it} - \overline{\varepsilon_i})$$

The random effects model estimates the following model assuming α_i is purely random. Hence, unlike the fixed effects model it is not consistent when patient specific unobservable are biasing the results (Cameron & Trivedi, 2010):

$$y_{it} = \propto_i + x'_{it}\beta + \varepsilon_{it}$$

A Hausman test compares two estimators where one is consistent under two hypotheses (H_0, $H\alpha$) and one is consistent only under one (H_0). If the two estimators are dissimilar, H_0 is rejected. In this case, if the fixed effects and random effects estimators are sufficiently different, then the hypothesis that there are patient specific factors biasing the results (H_0) is rejected. Under the null hypothesis (H_0), the following quadratic form approaches a chi-square distribution:

$$H = \left(\hat{\beta} - \beta\right)'\{\hat{V}(\hat{\beta} - \beta)\}^{-1}(\hat{\beta} - \beta)$$

Where $\hat{\beta}$ is the fixed effects estimator and β is the random effects estimator.

Included Variables

The question of interest for this chapter is the potential relationship between the number of LSPs in the PICU and other patients' LOS. As such, one key independent variable of interest is the LSP ratio (described above), as it effectively isolates the effect of LSPs on an individual's LOS independent of the general effect of an additional patient. Other control variables were included based on a consideration of what might confound the relationship between the LSP ratio and LOS.

Firstly, since this data analysis exploits the overlap in patient stays, it inaccurately summarizes the average number of other patients and LSPs when there is not information about every other patient present in the PICU over the patients' *entire* stay. This is the case for patients whose LOS started before (12 patients) or ended after (9 patients) the study period. Additionally, the longer these patients' stay, the less information is available regarding overlap with other patients, creating a bias. As such, two dummy variables Before Study and After Study were included.

Additionally, problems arise from the fact that LSP ratio is an average spanning different intervals of time. Regression to the mean implies that patients with longer LOS will be more prone to have an LSP ratio closer to the average, while the extreme values will tend to have lower LOS. To try and control for regression to the mean potentially confounding the relationship between LOS and LSP ratio, the top and bottom 5% of the LSP ratio were isolated into two dummy variables (High LSP Ratio and Low LSP Ratio).

It was considered that time variant unobserved variables may impact both patients' LOS and the number of LSPs in the PICU at any given time. To control for this, a series of 13 dummy variables indicating the patients' month at admit were included. Patients were admitted up two months before the study, leaving 14 months of admit and 13 variables (with one month as the baseline). The variables identified in the previous chapter that were found to have a significant impact on LOS were included.

Additionally, all models were estimated by replacing the LSP ratio with the numerator and denominator of LSP ratio as separate variables. This provides the more natural interpretation of the effect of an additional LSP (on average over a patient's stay) on LOS, controlling for the total number of patients. The only difference in the covariates

used in this model relative to the one above is the high and low LSP Ratio variables (to control for regression to the mean) were replaced with the four variables of the same type for high and low values of both the number of LSPs and patients per day.

3.2 Results

The results of three survival regressions with three separate parameterizations are presented below. The key covariate of interest is the LSP ratio. Other variables are included as controls. These results are discussed in chapter 4.

Table 3.1- Log-logistic, Weibull AFT and Cox results

	Log-logistic (AFT) Coefficient (SEs)	**Weibull (AFT) Coefficient (SEs)**	**Cox (PH) Hazard Ratio (SEs)**
LSP Ratio	-0.75** (0.32)	-1.45*** (0.34)	6.33*** (3.15)
High LSP Ratio	-0.52*** (0.19)	-0.90*** (0.22)	3.01*** (0.95)
Low LSP Ratio	0.09 (0.15)	0.01 (0.20)	0.96 (0.22)
Before Study	0.85*** (0.26)	0.92*** (0.27)	0.28*** (0.12)
After Study	0.63** (0.28)	0.26 (0.29)	0.59 (0.27)
Peripherally inserted central catheter	0.73*** (0.10)	0.87*** (0.10)	0.32*** (0.05)
Arterial lines	0.43*** (0.08)	0.32*** (0.08)	0.61*** (0.08)
Mechanical ventilation	0.55*** (0.08)	0.59*** (0.08)	0.47*** (0.06)
Non-invasive ventilation	0.68*** (0.08)	0.60*** (0.08)	0.45*** (0.05)
Nitric Oxide	0.45** (0.17)	0.23 (0.20)	0.78 (0.23)
Isolated during stay	0.39*** (0.08)	0.45*** (0.08)	0.55*** (0.06)
ECMO	1.26*** (0.48)	1.28* (0.71)	0.18* (0.18)
Operating Room	-0.23*** (0.08)	-0.21** (0.08)	1.36** (0.16
Ward	0.32***	0.40***	0.64***

	(0.12)	(0.12)	(0.11)
Ward Re-Admit	0.60*** (0.12)	0.58*** (0.12)	0.47*** (0.08)
Age<1	0.19*** (0.07)	0.22*** (0.08)	0.75*** (0.08)
PRISM	0.03*** (0.01)	0.03*** (0.01)	0.96*** (0.01)
Constant	-0.22 (0.80)	0.44*** (0.17)	-
Month at Admit (June 2015)			
Dec. 14	1.65*** (0.61)	1.23 (0.75)	0.19 (0.22)
Jan.	0.83*** (0.25)	0.87*** (0.27)	0.30*** (0.12)
Feb.	0.36** (0.16)	0.30* (0.17)	0.66* (0.16)
Mar.	0.14 (0.14)	0.08 (0.15)	0.85 (0.19)
Apr.	-0.01 (0.16)	-0.11 (0.16)	1.08 (0.25)
May	0.28* (0.15)	0.32* (0.16)	0.61** (0.14)
Jul.	0.09 (0.17)	0.12 (0.18)	0.82 (0.21)
Aug.	0.54*** (0.16)	0.37* (0.21)	0.57* (0.17)
Sept.	0.34** (0.16)	0.26 (0.17)	0.64* (0.16)
Oct.	0.37** (0.18)	0.10 (0.18)	0.81 (0.21)
Nov.	0.35** (0.16)	0.53*** (0.17)	0.48*** (0.12)
Dec.	0.21 (0.15)	0.21 (0.16)	0.75 (0.17)
Jan. 16	0.18 (0.16)	0.33** (0.16)	0.65* (0.15)
Feb. 16	-0.90 (0.78)	-0.33 (0.61)	1.85 (1.65)

Below are the results of the covariates included in table 3.1 in quantile and Laplace regressions.

Table 3.2 Quantile/Laplace regression results

ln(LOS)	5	25	50	75	95
Quantile: Coefficient (Bootstap SE)					
LSP Ratio	-1.07* (0.59)	-0.37 (0.38)	-0.34 (0.41)	-1.62*** (0.54)	-2.16*** (0.80)
High LSP Ratio	-0.64 (0.49)	-0.42 (0.33)	-0.31 (0.23)	-0.77*** (0.27)	-1.50*** (0.50)
Low LSP Ratio	0.41 (0.32)	0.04 (0.23)	-0.02 (0.20)	0.42* (0.26)	-0.03 (0.33)
Before Study	5.93*** (1.03)	4.23*** (1.03)	4.30*** (1.10)	2.15** (0.98)	2.08** (1.04)
After Study	1.59*** (0.37)	0.72* (0.42)	0.81**	0.44 (0.32)	0.08 (0.40)
Arterial lines	0.64*** (0.13)	0.50*** (0.12)	0.31** (0.13)	0.59*** (0.15)	0.22 (0.22)
Peripherally insterted central catheter	0.59*** (0.16)	0.79*** (0.17)	0.71*** (0.17)	0.74*** (0.18)	0.99*** (0.26)
Mechanical ventilation	0.15 (0.18)	0.38*** (0.10)	0.63*** (0.09)	0.66*** (0.12)	0.34* (0.18)
Non-invasive ventilation	0.88*** (0.14)	0.73*** (0.11)	0.66*** (0.13)	0.68*** (0.14)	0.44** (0.18)
Nitric Oxide	0.51 (0.37)	0.33 (0.34)	0.42* (0.23)	-0.04 (0.25)	-0.29 (0.24)
Isolated during stay	0.50*** (0.15)	0.32*** (0.11)	0.29** (0.12)	0.39*** (0.14)	0.60*** (0.17)
ECMO	-0.10 (0.68)	0.02 (0.74)	0.35 (0.71)	0.48 (0.60)	-0.02 (0.49)
Operating Room	-0.10 (0.16)	-0.07 (0.11)	-0.23* (0.12)	-0.44*** (0.13)	0.01 (0.22)
Ward	0.02 (0.29)	0.41** (0.20)	0.34* (0.18)	0.47** (0.20)	0.52* (0.30)
Ward Re-Admit	0.37 (0.23)	0.55* (0.19)	0.66*** (0.18)	0.55*** (0.20)	0.58** (0.27)
PRISM	0.02 (0.01)	0.02* (0.01)	0.02 (0.01)	0.01 (0.02)	0.05*** (0.02)
Age<1	0.08 (0.15)	0.12 (0.10)	0.18* (0.10)	0.20* (0.12)	0.36** (0.17)
Constant	-0.89*** (0.26)	-0.82*** (0.22)	-0.35 (0.22)	0.54 (0.33)	1.63*** (0.40)
Month at admit (June reference)					
Dec. 14	3,98*** (0.40)	2.82*** (0.30)	2.31*** (0.28)	1.95*** (0.36)	1.45*** (0.44)

Jan.	0.18 (0.57)	0.80* (0.48)	1.00*** (0.38)	1.39*** (0.48)	0.76* (0.44)
Feb.	0.19 (0.21)	0.36* (0.21)	0.35** (0.17)	0.42* (0.25)	0.18 (0.33)
Mar.	-0.02 (0.21)	0.23 (0.16)	0.21 (0.18)	0.18 (0.23)	0.01 (0.30)
Apr.	-0.29 (0.21)	0.05 (0.25)	0.02 (0.20)	-0.03 (0.28)	-0.57* (0.31)
May	0.17 (0.25)	0.45*** (0.17)	0.28 (0.19)	0.23 (0.26)	0.40 (0.35)
Jul.	-0.23 (0.29)	-0.04 (0.19)	0.12 (0.23)	0.20 (0.23)	-0.03 (0.29)
Aug.	-0.07 (0.50)	0.72** (0.30)	0.54** (0.22)	0.34 (0.26)	0.61 (0.48)
Sept.	0.27 (0.19)	0.39** (0.18)	0.34* (0.19)	0.47* (0.26)	-0.06 (0.40)
Oct.	0.43 (0.33)	0.62*** (0.19)	0.30 (0.20)	0.18 (0.31)	-0.15 (0.40)
Nov.	0.24 (0.27)	0.28 (0.21)	0.32* (0.17)	0.55* (0.32)	0.49 (0.38)
Dec.	0.30 (0.22)	0.29 (0.18)	0.11 (0.19)	0.33 (0.26)	0.10 (0.35)
Jan. 16	-0.47* (0.23)	0.11 (0.32)	0.15 (0.22)	0.50* (0.26)	0.23 (0.34)
Feb. 16	-1.95 (0.90)	-1.38 (0.96)	0.01 (1.03)	-0.20 (0.99)	-0.62 (1.09)
LOS	**5**	**25**	**50**	**75**	**95**
Laplace: Coefficient (Robust SE)					
LSP Ratio	-0.42 (0.55)	-0.73 (0.83)	-1.86** (0.90)	-4.74*** (1.52)	-11.07** (4.66)
High LSP Ratio	-0.81*** (0.52)	-0.78 (0.49)	-1.00* (0.52)	-3.19*** (1.21)	-6.89** (2.78)
Low LSP Ratio	0.25 (0.25)	0.13 (0.44)	0.29 (0.47)	0.85 (0.58)	3.34* (1.91)
Before Study	χ	χ	χ	χ	χ
After Study	3.58*** (0.64)	4.93*** (1.50)	6.74*** (2.15)	1.43 (1.27)	38.65*** (5.10)
Peripherally insterted central catheter	0.94*** (0.31)	2.50 (1.53)	4.76*** (0.84)	5.87*** (0.94)	17.13*** (3.40)
Arterial lines	0.63*** (0.15)	0.57*** (0.21)	0.73*** (0.25)	1.57*** (0.38)	0.37 (0.57)
Mechanical ventilation	0.44*** (0.13)	0.43** (0.19)	1.08*** (0.25)	1.78*** (0.40)	2.36*** (0.67)

Non-invasive ventilation	0.95*** (0.18)	0.91*** (0.290	1.60*** (0.38)	2.83*** (0.51)	3.93*** (1.09)
Nitric Oxide	0.23 (0.44)	3.42** (1.63)	2.96** (1.50)	4.95** (2.00)	-1.22 (0.94)
Isolated during stay	0.42*** (0.15)	0.45** (0.22)	0.80*** (0.28)	1.33*** (0.44)	3.59*** (1.18)
ECMO	4.79** (2.03)	4.25** (1.64)	4.36 (2.71)	6.05 (6.98)	8.17 (8.56)
Operating Room	-0.27 (0.14)	-0.24 (0.18)	-0.38* (0.23)	-0.49 (0.38)	0.73 (0.61)
Ward	-0.10 (0.35)	0.24 (0.53_	0.41 (0.57)	1.32 (0.94)	1.58 (1.38(
Ward Re-Admit	0.37 (0.35)	0.84 (0.59)	1.58** (0.70)	2.84*** (0.72)	15.10χ
Age<1	0.09 (0.13)	0.18 (0.21)	0.20 (0.23)	0.07 (0.35)	1.19 (1.03)
PRISM	0.02 (0.02)	0.05* (0.02)	0.06* (0.03)	0.12** (0.05)	0.24** (0.09)
Constant	52.67*** (0.27)	53.3*** (0.42)	53.84*** (0.70)	55.48*** (0.75)	59.46*** (2.35)
Month at admit (December 2014 reference)					
Jan.	-52.13*** (0.74)	-52.25*** (1.54)	-51.24*** (2.36)	-43.96*** (2.87)	-20.64*** (4.28)
Feb.	-52.69*** (0.26)	-52.59*** (0.37)	-52.32*** (2.04)	-52.29*** (0.56)	-52.96*** (1.72)
Mar.	-52.74*** (0.26)	-52.91χ	-52.87*** (2.06)	-53.42χ	-54.04*** (2.16)
Apr.	-52.89*** (0.31)	-53.04*** (0.34)	-53.32*** (2.11)	-54.20*** (0.61)	-56.19*** (2.77)
May	-52.57*** (0.27)	-52.57*** (0.34)	-52.42*** (2.08)	-52.96*** (0.62)	-52.99*** (1.86)
Jun.	-52.99*** (0.26)	-52.84*** (0.37)	-52.76*** (2.06)	-52.57*** (0.60)	-53.25*** (1.87)
Jul.	-52.91*** (0.25)	-52.86*** (0.32)	-52.85*** (2.05)	-52.87*** (0.62)	-53.77*** (1.86)
Aug.	-52.10*** (0.40)	-52.14*** (0.50)	-52.15*** (2.09)	-51.65*** (1.10)	-51.94*** (2.37)
Sept.	-52.19*** (0.24)	-52.53*** (0.34)	-52.39*** (2.07)	-52.42*** (0.57)	-53.28*** (1.98)
Oct.	-52.07*** (0.29)	-52.40*** (0.47)	-52.40*** (2.09)	-53.01*** (0.71)	-53.43*** (2.55)
Nov.	-52.67*** (0.32)	-52.63*** (0.37)	-52.24*** (2.05)	-51.71*** (1.13)	-49.22*** (3.28)
Dec.	-52.55*** (0.25)	-52.71*** (0.35)	-52.60*** (2.08)	-52.65*** (0.54)	-51.82χ
Jan. 16	-53.08χ	-53.03***	-52.57***	-52.14***	-53.65***

		(0.33)	(2.15)	(0.63)	(1.90)
Feb. 16	-61.66χ	-58.24*** (2.19)	-56.91χ	-54.32*** (0.75)	-86.38χ

*Significant at: ***<1%, **<5%, *<10%*

χ- omitted due to collinearity

A graphical representation of these results in provide in Appendix H

These regressions allow the effect of the LSP ratio to be assessed at different percentiles in the distribution of LOS. The results are discussed in chapter 4.

The results of three survival regressions with three separate parameterizations are presented below. The key covariate of interest is the average number of LSPs per day. Other variables are included as controls. These results are discussed in chapter 4.

Table 3.3- LSP per day results

Note: only the newly added variables of interest have been included in tables 3.3 and 3.4, as the effect of the other covariates are covered in the tables above and in Chapter 2

Coefficient (SEs)	Log-logistic (AFT)	Weibull (AFT)	Cox (PH)
LSPs per day	-0.23*** (0.06)	-0.33***(0.07)	1.59*** (0.16)
Patients per day	0.02 (0.03)	0.03 (0.04)	0.96 (0.05)

*Significant at: ***<1%, **<5%, *<10%*

Below are the results of the covariates included in table 3.3 in quantile and Laplace regressions.

Table 3.4- LSP per day quantile/Laplace results

ln(LOS)	5	25	50	75	95
Quantile: Coefficient (Bootstap SE)					
LSPs per day	-0.13 (0.10)	-0.16* (0.09)	-0.14 (0.09)	-0.25** (0.13)	-0.47*** (0.17)
Patients per day	-0.04 (0.04)	-0.02 (0.03)	0.01 (0.04)	0.03 (0.06)	0.10 (0.10)
LOS	**5**	**25**	**50**	**75**	**95**
Laplace Coefficient (Robust SE)					
LSPs per day	-0.19 (0.12)	-0.29* (0.16)	-0.45** (0.19)	-0.86** (0.37)	-2.97 (1.91)
Patients per day	-0.04 (0.04)	-0.03 (0.07)	0.01 (0.08)	-0.01 (0.15)	0.28 (0.27)

*Significant at: ***<1%, **<5%, *<10%*

These regressions allow the effect of the average LSPs per day to be assessed at different percentiles in the distribution of LOS. The results are discussed in chapter 4.

Table 3.5- Robustness check (fixed effects regression)

Number of observations- 116
Number of groups- 47
R^2 within: 0.22 R^2 between: 0.03 R^2 overall: 0.11

ln(LOS)	Coefficient	Panel robust standard errors	p-value	95% Confidence Interval
LSP Ratio	-2.30	0.97	0.022	-4.25-(-0.34)
High LSP Ratio	-1.50	0.60	0.016	-2.71-(-0.30)
Low LSP Ratio	0.32	0.41	0.445	-0.51-1.14
Before Study	0.90	0.65	0.175	-0.41-2.20
After Study	2.59	0.49	0.00	1.60-3.58

Table 3.5 above utilizes repeated stays to assemble an unbalanced "panel" to conduct a fixed effects regression. The results of this fixed effects regression are then compared to a random effects alternatives in a Hausman test presented in table 3.6 below. This allows for a robustness check regarding the existence of patient invariant bias. The results are discussed in chapter 4.

Table 3.6- Robustness check (Hausman test)

ln(LOS)	Fixed Effects	Random Effects	Difference	Standard Errors
LSP Ratio	-2.30	-2.09	-0.21	0.42
High LSP Ratio	-1.50	-1.32	-0.19	0.25
Low LSP Ratio	0.32	0.38	-0.06	0.23
Before Study	0.90	0.58	0.31	0.25
After Study	2.59	3.02	-0.43	0.88

H_0- difference in coefficients not systematic
Chi-squared- 2.53
p-value-0.7715

4 Chapter: Contribution to Understanding Long Stay Patients

This chapter discusses the results presented in the first three chapters. Firstly, this will examine how the results relate to: (i) a proposed framework for understanding LSPs, (ii) an ideal definition of LSPs, (iii) characteristics of LSPs and (iv) the impact of LSPs. Second, the conclusions of the discussion in the first section will be presented. Thirdly, the limitations of these conclusions will be discussed. Finally, potential implications of this research for care, policy, research and economics will be examined.

4.1 Discussion

A Framework for LSPs

To define and analyze LSPs, what is important about this group must be established. As discussed in Chapter 1, defining a cut-off for LSPs without a strong theoretical basis has led to heterogeneous definitions, a problematic outcome for research. The survey suggests that there are two distinct groups of interest within LSPs, high-need and high-dependency patients, and that any derived definition of LSPs should capture both groups.

The importance of defining LSPs was reinforced by the survey results, with 78% of respondents indicating this is important. However, 89% of respondents thought that if LSPs are defined, such a definition should include more than LOS. The open-ended responses of this survey provide suggestions as to what other elements should be included in the definition of LSPs.

The responses made it clear that there are different reasons patients might become "long-stay". Fourteen respondents identified patient condition (diagnosis, condition, stability ect.), 9 identified acuity/resource use, and 8 identified technology dependence

(full results in Chapter 1). This suggests that patients with the longest LOS but who differ in these respects should not be considered to be part of the same group.

However, this thesis asserts that it is not appropriate to abandon the use of LOS as the sole cut-off for defining LSPs. Firstly, defining LSPs by multiple factors would necessarily add complexity to the definition. Expert practitioners may not approve of this, as 9 of the 13 open-ended responses regarding methods for defining LSPs emphasized comparability, objectivity, and practicality or ease of use, all of which would be diminished with a more complex definition. Additionally, the top three ranked factors for a definition of LSP were consistency, usefulness and ease of use, while precision and exhaustiveness were ranked last. Arguably, a complex definition of LSPs would be more associated with the latter two factors and negatively associated with the former.

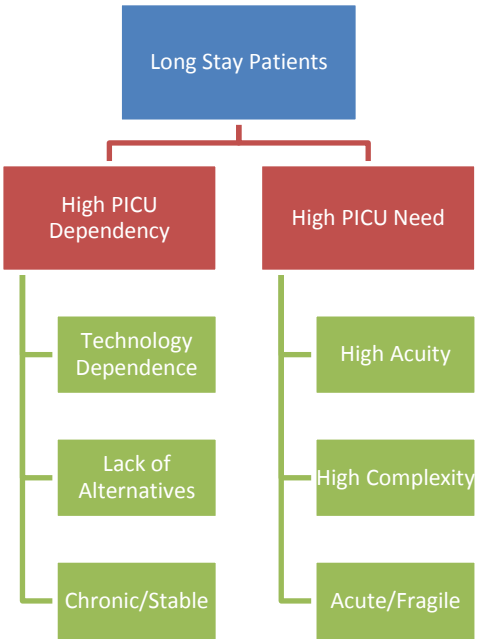
Additionally, from a purely conceptual perspective it may be difficult to justify continuing to use the term "long stay patient" when the definition does not solely rely on LOS. Indeed, if there is a group for which prolonged LOS is only one of many outcomes which distinguishes them, calling them "long stay" does not appear to be an entirely accurate label. In light of this, it appears that the group or groups that PICU that practitioners want to identify should be described by a term other than "long stay".

Therefore, this thesis proposes a theoretical framework that defines LSPs by their LOS, but then dichotomizes them into two separate groups: high-needs patients and high-dependency patients. This definition reconciles many of the key priorities identified above: it ensures that LSPs are the patients with the longest stays, is relatively simple, and it avoids the problem of inappropriately identifying two different types of patients as the same. Indeed, the idea that the patients with the longest stays are in fact two groups of

patients is embodied by one respondent; “in our PICU we believe it is better to define the category of long stay patients versus patients at the intermediate care level. The needs of these two groups are not the same”.

The characteristics of high-need and high-dependency patients were developed based on open-ended survey responses. High-needs patients are characterized by their high acuity, fragility, acute condition, high complexity and lack of stability. High-dependency patients are characterized by their technology dependence, lack of alternatives, stability and chronic conditions. Looking at the open-ended response in table 1.4, respondents made it clear that patients should be distinguished based on these characteristics. One respondent makes this contrast clear “some patients are acutely critically ill for long periods of time. This is different from a patient who is stable but technology dependent.”

Figure 4-1 A framework for LSPs



This distinction is also supported by the existing literature. Previous studies have noted the growing number of chronic patients in PICUs, and their relatively high risk of having prolonged stays (Briassoulis et al 2004, Edwards et al 2013). This has developed into a body of literature examining the chronically critically ill (CCI), an important part of the patient population in both adult ICUs and PICUs (Carmichael & Cheifetz 2012, MacIntyre, 2012). The CCI in the PICU are often characterized by long-term mechanical ventilation, and as such are closely linked to the proposed group of high-dependency patients. This provides support for the idea that there is a distinct subset of LSPs who have unique features and needs and are characterized by their chronic conditions and technology dependence.

Defining LSPs

Based on the framework established above, this thesis proposes a definition of LSP which uses LOS to identify both high-need and high-dependency patients. A sensitivity analysis presented in Chapter 2 finds that the ideal cut-off is at the 92nd percentile of LOS. For this patient population, that constitutes 42 patients whose stays exceed 13 days.

Unfortunately, the data gathering for this prospectively collected dataset pre-dates this survey, hence the information necessary to make the distinction between high need and high dependency patients is not available. However, a definition of LSPs was developed to try and include both groups of patients.

The results of the survey suggest that the ideal method for identifying the LOS cut-off for LSPs in any given PICU is using the percentile. Firstly, percentile was the highest ranked method among survey respondents. This ranking was statistically

significantly higher than all methods other than a pre-defined cut-off. Furthermore, percentile appears a better "compromise" than a pre-defined cut-off for those who emphasized the need for a definition to embody a specific hospital's circumstances. Indeed, the cross-sectional analysis in Chapter 1 indicated that those who showed a preference for subjective methods rejected a pre-defined cut-off, while they did not reject the percentile method. Therefore, using a percentile of LOS to identify LSPs is considered the preferred method according to the survey responses.

As outlined in Chapter 2, sensitivity analysis was used to identify the cut-off by assessing the predictive power of the definition on four outcomes of interest. This thesis considered that patients characterized by having a peripherally inserted central catheter for a prolonged period, or prolonged mechanical ventilation would be either high-need or high-dependency. Conversely, patients with large portions of their stays characterized by having an arterial or central venous lines should have longer than average stays, but not be LSPs. Therefore, the definition should be as predictive as possible of the first two variables, while having little predictive power or predict a negative relationship with the second two variables.

Notably, the 95th and 90th percentile of time with these two interventions were chosen based on inspecting histograms of frequency. Of course, this rather arbitrary cut-off suffers from the same weaknesses as previous definitions of LSPs which have been identified. Unfortunately, for practical purposes such decisions must be made at some stage, creating a limitation in this definition of LSPs.

The results of this sensitivity analysis are available in table 2.2. These results suggest that the 92nd percentile is the ideal cut-off point. It is the most predictive of

mechanical ventilation, and very close to the most predictive percentile for having a peripherally inserted central catheter. Notably, this definition is similar to the 95th percentile cut-off point used in some previous studies (Marcin et al, 2001; Ruttimann & Pollack, 1996). However, the sensitivity analysis indicates that using the 92nd over the 95th percentile may be consequential, as the area under the ROC curve drops from 0.97 to 0.84 for predicting prolonged mechanical ventilation.

For this dataset, this implies a definition of LSP of a stay greater than 13 days. Survey respondents who specifically mentioned the definition in their own PICU identified >10 days as beyond the 90th percentile (Sick Kids), >7 days (IWK), and >14 days (McMaster). This implies that the distribution of at least two of these PICUs may be able to easily accommodate this definition of LSPs.

Identifying and Discussing the Characteristics of LSPs

Having a better understanding of the theoretical framework and definition of LSPs provides the basis for evaluating their characteristics. The results of this analysis are found in Chapter 2. The identified characteristics are similar to those found in past studies. However, no previous studies in the literature simultaneously applied survival analysis, logistic regression and quantile analysis to their patient population. The results of this research suggest that the heterogeneity in LOS and the lack of certainty regarding the underlying risk process of patients' discharges imply significant value added to applying this mix of methods rather than selecting just one.

This analysis finds that the strongest predictors associated with both LSPs and longer LOS are the specific interventions that they receive. Indeed, interventions constituted 7/14 significant predictors of LOS and 4/5 significant predictors of LSPs.

Additionally, the magnitude of these coefficients suggest that they are important predictors of LOS/LSP with coefficients/odds ratio as large, or larger than other predictors. Given the discussion of high-need and high-dependency patients above, the strong predictive power of these variables should not be surprising. This framework suggests that the primary reasons for long stays are related to either technology dependence or a requirement for a high volume of PICU care. Both of these factors would be reflected in the interventions patients receive.

The other main category of predictors of LOS was the location from which the patient was admitted. Compared to the reference group of patients admitted from emergency and other hospitals, operating room patients had shorter stays, while ward patients, particularly re-admits from the ward, had longer stays. Patients with certain conditions and care requirements are likely both to have varying LOS and be concentrated in certain areas before being admitted to the PICU. In particular, re-admits from the ward, the best predictor in this class of variables, may be associated with the CCI (Carmichael & Cheifetz 2012). Indeed, this is the only one of these variables that adds predictive power to LSP as an outcome in the binary regression.

The remaining predictors of LOS are a patients' PRISM score and age less than one year. On average, a higher PRISM score leads to a higher LOS, consistent with the idea that patients at higher risk require more care. Additionally, on average patients under 1 year old have longer stays. Neither of these variables are significant predictors when extended to LSP as an outcome, although age<1 and PRISM>11 add predictive power.

Finally, one factor, medical cardiac, is highly predictive of being an LSP and not LOS. However the sample size for this group is very small (11 patients) and has a *very*

large standard error (see table 2.4) so it may be the case that this relationship is statistically, but not clinically significant.

Turning to the quantile and Laplace regressions, many of the variables are no longer significant at different quantiles. Unfortunately, differences between these models and the log-logistic AFT model may arise from many factors, and so it is perhaps best to avoid comparing them directly. However, they remain complementary methods as comparing the results between quantiles can be informative regarding the heterogeneity underlying the AFT estimates.

A visual inspection of graphs illustrating how each coefficient varies with the percentile (Appendix G) does not indicate that any of the variables follow a clear functional form (ie. obviously increasing or decreasing with the percentile of the outcome). However, there are many notable departures from the average effect reported by the regression at the median, which are discussed below. Additionally, many variables not specifically noted below had fluctuations around the median coefficient not following any particular pattern.

In both the quantile and Laplace regressions, having a peripherally inserted central catheter and being isolated during admission generally rise in their effect towards the end of the distribution (consistent with their predictive power of LSP). Additionally, the effect of mechanical ventilation and ward appear to be notably weaker at the start of the LOS distribution, while the effects of arterial line and nitric oxide appear notably weaker at the end of the distribution.

Discussing the Characteristics

The fluctuations in the quantile and Laplace regressions imply that the coefficients reported based on the mean value from the AFT model disguise underlying heterogeneity. Therefore, while the average effect of a covariate on time expressed at the average may still be the best summary of the effect of that variable, if any specific variable is of interest, it should be investigated further to better understand its full effect. Indeed, this is the approach that was taken in Chapter 3.

In terms of predicting LOS for practical purpose, some of the notes above regarding departures of the variable from their linear estimates should be considered. For example, perhaps a patients' status on mechanical ventilation or admission from the ward should not play a large role in predicating future LOS until the patient's stay passes a certain threshold. Similarly, presence of an arterial line and use of nitric oxide may only be predictive of longer LOS up to a certain point. More generally, empirical methods such as cubic spline that more directly model underlying heterogeneity may be helpful (Durrleman & Simon, 1989).

The tests of goodness of fit produce promising results. Examining figure 2.1, perfect fit of the AFT model should have the cumulative hazard function of the Cox-Snell residuals as a straight line (Cleves et al, 2010). Given that some variability around the line is expected, particularly in the right tail, these results illustrate a good fit to the data. For the logistic regression model, the average area under the ROC curve was 0.92 for the testing sample and 0.89 for the verification sample. Given the range of values possible from 0.5-1 this indicates an encouraging degree of predictive power. However, the size in the standard errors of the predictors, particularly in the logit model, serve as a reminder that considerable uncertainty remains, and the results of this single centre study are most

appropriately viewed as hypothesis generation and in tandem with results from the literature.

Revisiting the results from *Ruttiman and Pollack* and *Marcin et al* (see chapter 2), the results of these two models seem generally consistent with the literature. With the exception of emergency admit and CPR before admission, all of *Marcin et al's* variables available in this dataset are predictive of either LOS or LSP. The fact that some of the data used for this thesis (age < 1, PRISM score, postoperative status) are only significant when examining LOS and not LSP may be a factor of losing information when moving from an interval to a binary variable, since these variables are significant in *Marcin et al's* much larger sample. However, this may also be a factor of the specific interventions available in CHEO's data not used by *Marcin et al*. Indeed, this is supported by the fact that both PRISM > 11 and age < 1 have a significant relationship with LSP until included in a single regression with the intervention dummy variables, and both still add predictive power to the model.

Identifying and Discussing the Impact of LSPs

This analysis finds support that on average, when there are more LSPs in the PICU, patients have shorter stays. This difference is both statistically significant and important in magnitude. An economic analysis of these results suggests that there is a possible congestion effect which induce hospitals to ration the resources made available to patients.

Identifying the Impact of LSPs

The first and most notable result of this analysis is that the ratio of LSPs to total patients in the PICU is significantly associated with a decrease in LOS. This is true at the

5% level for both the log-logistic and Weibull parameterization of the AFT, the Cox PH model, the quantile regression at the 75th and 95th percentiles, the Laplace regression at the 50th, 75th, 95th percentiles and in the fixed effects regression used as a robustness check.

Therefore, within this hospital under the time of study, when there were relatively more LSPs as a share of total patients in the PICU during a patient's stay, that patient's stay was shorter. While potential issues with violating the PH assumption or imposing incorrect parameters were raised in Chapter 2, this result is robust to which model is used and hence the assumption under scrutiny.

From the quantile and Laplace regressions, this effect appears much stronger amongst patients with longer stays. Indeed, the estimated effect of the LSP ratio is more than 6 times larger at the 95th percentile relative to that at the median.

The size of the coefficients can be misleading or difficult to interpret. For each model, the coefficient indicates the effect of moving from an LSP ratio of 0 (no LSPs) to 1 (only LSPs). Of course, the effect of such a dramatic change is not of particular interest. Hence while the LSP ratio may be preferred for correctly identifying if LSPs have an effect on LOS independent of the total number of patients, it may be ideal to alter the model to more directly observe the magnitude of this effect.

Therefore, the easier to interpret coefficient provided in tables 3.3 and 3.4 which use the average number of LSPs per day are used for the discussion below. These results suggest that the number of LSPs in the PICU not only have a statistically significant effect, but a practically important one. Indeed, converting the semi-elasticities of the AFT models to percent change shows that when there is an additional LSP, the average

patient's stay is 15% shorter in log-logistic and 27% shorter in the Weibull. The Cox PH model suggests that at any given time, a patient who has one more LSP over their stay on average is 1.5 times more likely to be discharged from the PICU at any given time.

In the quantile regression, the association between LSPs and LOS appears to be generally increasing in LOS. The largest impact is at the 95th percentile, where a coefficient of -0.47 implies that one additional LSP per day over a patient's stay is associated with a 38% percent shorter stay on average. Considering the average patient in the 95th percentile has an LOS of 28.72 days, this implies that if the PICU has on average one more LSP, the patients' stay would be 10.9 days shorter. Finally, the Laplace regression suggests that a group with one more LSP per day would have 95% of its patients discharged 3 days earlier than a group with one less LSP per day.

Ultimately, the key result to draw from this analysis is that more LSPs in the PICU at a given time are associated with other patient's stays being shorter in both a statistically and practically significant way. This association is strongest amongst other patients with long stays. The key result from the robustness-check is that there do not appear to be patient-specific unobserved factors biasing the result. The Hausman test comparing this model to a random effects model produced a chi-square value of 2.53, and a p-value of 0.77, indicating the null hypothesis that patient-specific bias does exist could not be rejected. Of course, this conclusion is limited by the unrepresentative nature of the group with repeated stays, and the unbalanced/inconsistent nature of this longitudinal data.

Discussing the Impact

A review of the literature found no previous work investigating the relationship between LSPs and the stays of other patients. As such, there is not an established theoretical mechanism to describe this relationship. Therefore, to help better contextualize these results, this thesis will use the lens of the economic literature on peer effects to consider how LOS may be conceptualized from the perspective of the PICU. This is a hypothetical discussion of what theoretical mechanism *may* underlie the observed association, and does not necessarily imply that there is *any* causal mechanism underlying this relationship.

In a seminal paper in the peer effects literature, *Manski* characterizes three hypotheses often used to explain why "individuals in the same group behave similarly": exogenous effects, endogenous effects and correlated effects. Previous work has applied this framework to the effect of one patient's outcomes on another in an acute care hospital setting (Yakusheva 2017). This thesis does not apply the same approach as the peer effects literature. This thesis examines an average of other patients' outcomes for each given patient and therefore does not fit into the reference group/network structure generally applied to these problems, as each patient has a unique reference group (Bramoullé,et al. 2009). Hence, the association between LOS and LSPs in the PICU cannot be wholly characterized as the observation of any of *Manksi's* three effects. However, it is useful to consider which (if any) of these three effects may be the key driver of the observed association.

Exogenous effects imply an individuals' outcome varies with the exogenous characteristics of the group. Consider all the patients in the PICU at a given time to be a

"group". To reconcile with the data, this would imply that the characteristics of some such "groups" inherently lead to both more LSPs and shorter stays on average.

Endogenous effects occur where an individuals' outcome varies with the outcome of the group. To explain the association observed in the data, this would imply that all else equal, some characteristic of LSPs directly shorten the stays of other patients.

Finally, correlated effects occur where individuals in the same reference group have similar outcomes because they have similar characteristics or face similar institutional environments. This would imply that certain PICU environments are characterized by both more LSPs and shorter average stays.

Exogenous effects seem an unlikely explanation both because of the nature of the reference group and the negative spillover effects being discussed. Firstly, given that each patient has a unique reference group, it is unclear that there is any set of inherent characteristics associated with one "group" but not others. Furthermore, it is difficult to conceptualize an exogenous factor which leads to more LSPs, but shorter stays.

Based on existing evidence, endogenous effects appear more plausible. *Yakusheva* finds that patients who share a room with less acutely ill roommates receive less care, have shorter LOS and have lower costs *without* any observed negative effects on clinical condition or risk of being admitted. A descriptive study finds that pre-operative patients assigned a post-operative roommate have less anxiety and shorter post-operative stays (Kulik, Mahler & Moore, 1996). While it may not be the case that LSPs are "healthier" it is at least plausible that they are less *acutely* ill (ie. more stable), and their experience in the PICU setting may be akin to the effect of post-operative roommates.

However, in an online appendix *Yakusheva* estimates a model closer to the one estimated in this thesis which shows that the average health of the entire unit (rather than just the roommate) has statistically insignificant effects with *opposite* signs on all outcomes including LOS. Therefore, even if LSPs were the type of patients which have these kind of endogenous effects (which it is not clear they are) it does not appear that this kind of endogenous effect would apply to the entire PICU, particularly given that all the beds in CHEO's PICU are in separate rooms.

Notably, the reason *Yakusheva* estimates the model which is similar to the one used in this thesis is as a robustness check for the existence of correlated effects. In this way, this thesis' model may act partially as a test for correlated effects. Indeed, this thesis proposes that correlated effects are the most likely explanation for the observed association: if more LSPs in the PICU cause *congestion*, then it might be expected that the LOS of other patients in the PICU fall.

To see why, consider LOS as an *output* of the hospital. Economic theory suggests it is possible to view a "patient day" in the hospital as both an input and an output (Zweifel, Breyer & Kifmann, 2009). *Yakusheva* characterizes it as an input, and argues patients' LOS would be shortened if their health production function is exogenously shifted out by the presence of other patients with positive spillovers. However, since LSPs having this kind of spillover in this setting has already been dismissed, this thesis will examine the implications of treating a patient day as an output, where each patient day represents an additional unit of care that the patient receives.

According to this view, a reduction in LOS caused by additional LSPs could be viewed as the rationing of an output. Without developing a formal theory, consider a

simple case where the objective of the PICU is to maximize some weighted function of all individual LSPs' health production functions by choosing a share of some fixed, LSP specific output (ie. LSP days) to divvy up between individual LSPs in the PICU. It is obvious that the more LSPs that this fixed output must be divided between, the less of the output each LSP will receive. If LSPs' health production functions are increasing and concave, this also implies LSPs will be discharged with fewer "units of health".

Essentially, this theory posits that the PICU is constrained by the amount of the output (patient days) it can deliver at any given time, and hence is forced to reduce the number of patient days each patient receives when there are relatively more LSPs present. This rationing of patient days when there are more patients in the PICU could be described as a congestion effect.

In general, the evidence used for this thesis supports this theory. The results of Chapter 2 highlight that LSPs receive specific interventions at far higher rates than the rest of the patient population. If the PICU is only equipped to administer such interventions to a limited number of patients, this supports the notion that there is some kind of fixed LSP-specific output which must be rationed. Indeed, this is reinforced by the fact that these congestion effects are observed to be strongest amongst patients with the longest stays: in other words, the patients that most commonly require access to the interventions potentially being used by other LSPs. Hence, a theoretical analysis suggests that one explanation for the observed negative correlation between the number of LSPs in the PICU and LOS could be congestion effects, which under the peer effects framework would be characterized as driven by correlated effects.

4.2 Conclusions

This thesis has marshalled new and valuable information, including a survey of expert practitioners and a unique PICU dataset. It analyzed this information in both established and new ways, generating interesting conclusions regarding the best way to understand LSPs in the PICU. The characteristics of LSPs and longer LOS were similar to those in the established literature and identified valuable information regarding the use of methods to assess LSPs and LOS. The two primary conclusions of this thesis are a new theoretical framework and the identification of potential congestion effects.

Characteristics

For the most, the analysis of characteristics of LSPs in the PICU finds similar factors to those found in the literature, but is the first work to identify these factors in the Canadian context. In addition, this analysis highlights the heterogeneity of different covariates' effects on LOS. By using an AFT model, logistic regression and quantile/Laplace regression, this analysis illustrates that there is significant value added to simultaneously using all three of these approaches given the heterogeneity of patients and the particular relevance of LSPs.

Theoretical Framework

One key conclusion of this thesis is the creation of a proposed theoretical framework for LSPs which divides them into high-need and high-dependency patients. The literature has acknowledged the importance of LSPs, and that this group is increasingly being made up of, and even driven by patients with chronic conditions (Briassoulis, 2004; Carmichael & Cheifetz, 2012). However, the survey results obtained for this thesis emphasize the importance of explicitly making this distinction within a

definition of LSPs in the PICU, which a review of the literature suggests has not previously been done in empirical studies.

Making this distinction could increase the relevance of LSP research on resource management. Resource management has been identified as an important reason for defining LSPs both in the survey and the literature (Marcin et al., 2001; Naghib et al, 2010; van der Heide, 2004). However, the acuity and resource use of patients with long stays may vary significantly. In particular, the group being defined as high-need require more intensive PICU care than those patients that are high-dependence. Therefore, effectively distinguishing between how much of a long stay population is represented by both groups will be instructive for understanding the current and future resource use of PICUs.

This framework may also contribute to modelling care. Determining models of care was identified by survey respondents as one of the most important reasons for defining LSPs. Furthermore, many survey respondents indicated that a distinction similar to the one developed between high-need and high-dependency patients would be important in considering how to model care. Therefore, one interpretation of the survey responses is that a fundamental reason for identifying long stay patients is to identify alternative methods of care, but that how appropriate such alternative care will be depends on the patient's specific characteristics above and beyond their LOS.

Identifying a patient as having a high probability of having a long LOS based on their characteristics may not be sufficient for identifying their optimal "pathway of care". The established framework suggests that simply labelling that group as "long stay" may not be optimal. Instead, dividing LSPs into high-need and high-dependency patients and

individually identifying the characteristics each group might significantly contribute to understanding LSPs from both a resource and care perspective.

Congestion Effects

Another key conclusion of this thesis is the identification of potential congestion effects. This broadens the scope of understanding LSPs beyond their characteristics and outcomes to potentially assessing their impact.

In particular, the evidence of congestion effects suggests that identifying alternative care options for high-dependency patients (discussed above) would have wide ranging implications. Bringing these patients outside the PICU may allow them to receive care more suited to their needs. Additionally, the potential existence of congestion effects suggests it would also reduce the need for the PICU to ration the resources given to the high-need patients remaining in the PICU, also improving their care. Congestion effects suggest that LSPs should not only be understood in terms of their own characteristics and outcomes, but also in terms of the impact they may have on other patients.

4.3 Limitations

While this thesis identifies key conclusions to be drawn from this analysis, it is important to be mindful that these results and conclusions are based on limited evidence. It is important to consider these limitations before considering the implications of these conclusions.

One limitation of this analysis is applicability to other centres, as it relies on the assumption that the survey and patient data are representative. The data used for the characteristics of LSPs, the identification of congestion effects and the definition of LSPs comes from a single PICU in a single year. Hence, any of the conclusions drawn from

these analyses may not be applicable to other centres. Particularly the applicability of congestion effects, which have not been explored by previous research, should be interpreted tentatively. Additionally, this representativeness is a concern for the definition of LSP which was set at the 92nd percentile based on sensitivity analysis. The same analysis may find different results when applied to a larger number of centres.

Furthermore, it should be noted that certain expert opinions in Canadian PICUs were underrepresented. In particular, the results of this survey do not represent the views of French-Canadian PICUs as strongly as other parts of Canada. However, it is notable that the respondents for this survey were targeted because of their specific expertise, rather than their representativeness of any given population. Hence, the survey respondents achieve the goal of providing specific expert insight from PICUs across all of Canada.

Another limitation of these conclusions is the observational nature of the data. Particularly for the analysis of the characteristics of LSPs, the coefficients of the predictors should be interpreted as the "association with" rather than the "effect on" the outcome. It should be noted that the goal of this analysis is to identify the factors most predictive of the outcome, making associations between the predictors and the covariates rather than the effect of primary interest.

The observational nature of the data is more concerning for the exploration of congestion effects. Here there was an effort to control for potential confounders such that the effect of the LSP ratio or LSPs per day on LOS can have as causal an interpretation as possible. Indeed, the discussed theoretical mechanism which attributes the observed association to "congestion effects" is premised on the fact that this relationship is causal.

Therefore, it is an important limitation that some relevant control variables could have been either overlooked or unavailable. The potential for such an omission serves as a reminder that any direct relationship suggested by the observed association remains theoretical.

Furthermore, the analysis of these results may suffer from the endogeneity[1] inherent in measuring peer effects. Described by *Manski* as the "reflection problem", this simultaneity problem arises from the fact that the outcome of interest (LOS) is partially determined by the number of LSPs, which is in turn also partially determined by the outcome (as patient's LOS partially determines the number of LSPs). Notably, even if the peer effects are mostly a function of correlated (as oppose to endogenous or exogenous) effects as proposed above, since the differences in the common environment are driven by the number of LSPs, which is in turn determined by the LOS of other patients, the patients' own LOS still appears on both sides of the regression equation and the problem of simultaneity persists.

However, it is notable that this is ultimately a problem of exact identification of peer effects, rather than their existence. If these peer effects do exist, then by definition the endogeneity problem is no longer an issue. Hence, the potential for this issue does not diminish the fact that this data presents evidence of the existence of potential congestion effects. Notably, *Angrist's* critique of peer effects models should not apply in this case where each observation has a unique reference groups and the association under discussion is actually negative (Angrist, 2014).

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[1] When an explanatory variable is correlated with the error term

Finally, despite presenting a framework for dichotomizing LSPs, how appropriate this dichotomization is could not be empirically affirmed, nor could the specific characteristics of high-need and high-dependency patients be identified. In general, being able to empirically compare separate groups of LSPs by the characteristics of high-need and high-dependency patients will be important to identify the usefulness of this dichotomization. Additionally, while this framework was developed from the responses of expert survey respondents, this does not necessarily imply that such a framework would be accepted by practitioners.

4.4 Implications

The conclusions outlined above have potential implications for care, policy, further research and economics. Of course, such implications are relevant only to the extent to which one accepts the conclusions of this paper, which are inherently limited by many of the factors discussed above.

Regarding care, the key implication of the results of this thesis is that high-dependency patients should be defined, identified, and given care suited to their needs. A growing body of literature regarding designing specific models of care for the CCI in the PICU and their families may be transferable to high-dependency patients (Marcus, Henderson and Boss, 2016).

Additionally, the potential existence of congestion effects suggest that modelling care in this way would not only benefit high-dependency patients, but also positively effect the high-need patients still in the PICU. If high-dependency patients can begin to receive more care outside the PICU, this reduces the need for the PICU to ration resources for the remaining patients.

Regarding research, it will be important to explore the proposed theoretical framework further. Before accepting this framework, research that is able to empirically identify the characteristics of high-need and high-dependency patients will be important. Ideally such research could span multiple PICUs. Additionally, it may be ideal to more systematically consult practitioners on their views of this framework, for example using the Delphi method (Linstone & Tuoff, 1975).

Additionally, while there appears to be a strong negative correlation between LOS and the number of LSPs in the PICU, the basis of this correlation in observational data implies significant room for future research. Indeed, more research dealing with the endogeneity effects of measuring spillovers discussed above, controlling for a broader range of potential confounders, and applying a different array of empirical methods would strengthen the observed association and perhaps create a stronger picture of the underlying relationship. Furthermore, research of the existence of these effects in other PICUs will be important as it is unclear how representative CHEO is of other centres, particularly other centres who have separate areas for LSPs or otherwise differently structure their care for LSPs.

Thirdly, as identified above, these research findings suggest that the key implication for care and policy are that alternatives to the PICU should be developed for those LSPs that would benefit from this. However, while this research is explicit in identifying the potential negatives of caring for high-dependency patients in the PICU, it does not as explicitly identify which alternatives to this are preferable. Investigating this, perhaps using the difference in care and congestion effects in PICUs that identified having a separate area for LSPs in the survey, may be telling in this regard.

Finally, the results of this thesis may have interesting implications on the economic theory surrounding the management of hospital resources. Any economic model which aims to identify the optimal use of scarce hospital resources depends on the appropriate identification of costs and benefits (Zweifel, Breyer & Kifmann, 2009). In this way, the new theoretical framework for LSPs may helpful in understanding the costs and benefits of different investments which aim to help LSPs.

Even more pertinent to conducting this kind of economic analysis is the identification of potential congestion effects. Firstly, to the author's knowledge this is the first indication of the potential for such effects in an intensive care unit, in a pediatric hospital setting, or in Canada. These settings all present unique incentive structures, and therefore comparing how decisions are made regarding congestion in these settings relative to others could be particularly informative for economic theory. Indeed, while some intuition for the theory behind congestion effects was briefly explored above, this kind of inductive theory could be developed more formally using more data.

Furthermore, despite examining a related concept, the data analysis in this thesis asks a very different question from that which is asked by the large and growing health economics literature on peer effects (Bramoullé et al., 2009; Fortin & Yazbeck, 2014 Golberstein, Eisenberg & Downs, 2016; Yakusheva, 2017). Such work generally focuses on identifying reference groups to examine and break down similarities between group members. Such an approach is particularly useful in separating endogenous, exogenous and correlated effects. However, while this thesis focuses on correlated effects, it appears that the goal of many papers is often to try and *remove* correlated effects (Bramoullé et

al., 2009; Manski, 1993; Fortin & Yazbeck, 2014; Sacerdote, 2001; Yakusheva, 2017; Zimmerman, 2003).

While the limitations of this thesis' results to solely identify correlated effects have been made clear, they emphasizes the potential for using data on individual outcomes to try and understand effects at an institutional level. Indeed, while previous studies have focused on endogenous effects because of their potential for causing "multipliers", it may be the case that correlated effects are more amenable to being shaped by policy. Additionally, this analysis explicitly identifies the potential for a type of peer effect which occurs because of a peer's direct effect on a shared environment. While this thesis assumes this is most associated *Manski's* correlated effects, more explicitly exploring this unique type of peer effect may be interesting grounds for future economic analysis.

Hence, while the exact effect of a peer on an individual's outcome is interesting, these results suggest that how a peer influences other factors could be equally important. For example, while the commonly studied potential for obesity-related endogenous peer effects are certainly interesting it may *also* be interesting to use this type of data to understand how obese individuals shape their environment. For example, a more obese population may shape the nutrition options available at the school or community level.

As a final note, the approach of this thesis in which each patient has a unique reference group may have interesting implications in light of the critique of peer effect models made in *Angrist 2014.*

Ultimately, this thesis makes an effort to contribute to the current understanding of LSPs in the PICU. Particularly when discussing children requiring intensive care, few

would deny that the best information available should be used at all levels of decision making in our healthcare system to deliver the best care. Hopefully the results of this thesis will contribute to that wealth of information.

Appendices

Appendix A

A Survey of Expert Practitioners on Defining Long Stay Patients in the Pediatric Intensive Care Unit

Pediatric intensive care units (PICUs) are a costly component of the healthcare system. This cost is related to PICU patient length of stay and to the resources that PICU patients require. It has been noticed that a small number of patients in the PICU consume a disproportionate amount of the resources. These patients have been referred to as "long stay patients". However, there is currently no standardized definition for a long stay patient. The purpose of this survey is to determine your thoughts on defining this patient population.

A. <u>Demographic questions:</u>

The following questions relate to you and the PICU in your hospital.

1. What is the name of your PICU/hospital? _____
2. What is your position in the PICU? _____
3. In what year did you start in your current position?
   _____
4. What is the highest level of education you have completed? In what year did you graduate? _____
5. In what year were you born? _____
6. What is your gender? _____
7. How many beds does your PICU have? ***(select ONE answer only)***

- o < 5
- o 5-10
- o 11-20
- o Other _____
  _____

8. How many patients are admitted to your PICU per year? ***(select ONE answer only)***

- o <200

- O 201-400
- O 401-600
- O 601-1000
- O 1001 – 2000
- O Unsure
- O Other

_____
_____

9. Does your hospital have a separate area for long stay patients?

- O No
  - O Our hospital has plans to have a separate unit
  - O Our hospital has no plans to have a separate unit
  - O I am unaware of any future plans in this regard
- O Yes
  - O Designated beds in the PICU
  - O Specialized unit separate from but adjacent to the PICU
  - O Specialized unit in an entirely different location than the PICU
  - O Other

_____
_____

B. <u>Definition of long stay patients</u>

The following questions relate to the definition of long stay patients in the PICU.

1. Do you believe it is important to define a distinct group of "long stay patients" that have longer than the average stays in the PICU?
   - O No
   - O Yes
   - O Unsure
   - O Comment

   _____
   _____

2. If you answered yes to the above question, please check off the reason(s) why you believe it is important to define long stay patients in the PICU (check all that apply).
   - O To determine current PICU resource utilization

- O To determine future PICU resource needs
- O To determine nursing staffing needs
- O To be able to compare PICU length of stay data across units
- O To gather data to determine alternate models of care for these patients
- O Other_____

_____

3. Do you believe there are components *other* than a patients' length of stay that should be considered in the definition of long stay patients in a PICU?

   O No

   Comment_____

   _____

   O Yes

   Please specify:

   _____

   _____

4. Which characteristics should a definition of long stay patients embody in order to be the *most valuable* to you (rank from 1 to 6)?

   ☐ **Exhaustive** (captures *all* long stay patients)

   ☐ **Precise** (capture *only* long stay patients)

   ☐ **Consistent** (across different PICUs)

   ☐ **Flexible** (adapts to different circumstances in different PICUs)

   ☐ **Useful** (to the work you do in the PICU)

   ☐ **Easy to use** (in the context of your work in the PICU)

5. **Methods**: *Please rank the following methods **from 1 to 5** based on which you feel would best determine the group of patients that would be defined as long stay patients. Where possible, identify what you consider to be the strengths and weaknesses of each method.*

   - **Local Consensus** - with the aid of graphs and other information, each PICU decides what group is considered long stay patients based on their own judgment.
   - **Multiple of the average-** those with stays longer than some multiple of the average (eg. 5 times the average).
   - **Percentile**- patients with stays beyond a certain percentile (eg. beyond the 95th percentile, or the 5% of patients with the longest stays would be "long stay").

- **Share of resources**- the smallest number of patients using the most resources (eg. if 15% of patients used 50% of resources, this group would be considered "long stay").
- **Pre-defined cutoff**- patients exceeding a specified length of stay would be considered "long stay" (eg. all patient with stays longer than 10 days).

Method	Rank	Strengths and/or Weaknesses
Local Consensus		
Multiple of the average		
Percentile		
Share of resources		
Pre-Defined Cutoff		

Please contribute any other information, ideas or comments you have regarding the definition of long stay patients in a PICU.
Response:

Appendix B

Hospital	Responses
Alberta Children's Hospital	3
British Columbia Children's Hospital	2
Centre hospitalier universitaire de Quebec	0
Centre hospitalier universitaire Sainte-Justine	2
Children's Hospital of Eastern Ontario	3
Children's Hospital of Western Ontario	1
IWK Health Centre	2
Janeway Children's Hospital	3
McMaster Children's Hospital	3
Montreal Children's Hospital	2
Royal University Hospital	1
Hospital for Sick Children	2
Stollery Children's Hospital	2
Winnipeg Children's Hospital	2

Appendix C

Quote
change in practice- ie novel therapies that change the paradigm for children with SMA for example or Congenital Hearth Disease- extending life and time in ICU difficult to get reliable data locally and across different sites.
This is a complex and unique subset of Pediatric ICU patients. Another reason to identify this patient population would be to put in place processes specific to the care of these patients, for example defining a pathway of care which would outline specific medical and other health care team member consults that should be considered on or before a specified time frame to support early discharge/transfer planning.
Taking 2around the 10th to 90th centiles beyond the mean and excluding the outliers that skew the data, then LOS is prolonged in our PICU if > 10 days and in the CICU if > 15 days. There must not be an arbitrary number set by a regulatory agency (such as MOH), which is always generated by static numbers and without context. This is a mistake and only looks at the cost factors, and not resource or social determinants.

A definition is necessary for effective benchmarking of comparative patient populations, and to define the reasons for increased LOS.
It will be important to consider what the purpose of identifying these patients are. Once this is known, then it may be easier to determine the definition. Consideration would have to be given to available alternatives if the aim is to move these patients from intensive care environments. Subjective would probably be the most useful as it could be defined in the context of the individual institutions
Given the short mean length of stay normally associated with PICU admission, I think that time alone will identify these patients as atypical and can think of no better marker. We have introduced a definition of 7 days and approach these patients with a view to rationalise resource use and hold meetings to ensure that we remained focus on the goals of care.
“if long stay patient has acute events, that is not long stay”
“We would look at stability of the patient and need for critical care interventions to determine reason for transfer to a patient care area that specializes in long term care”
« Dans notre service nous croyons qu'il serait bien de définir la catégorie <<patient long terme>> versus patient de niveau de soins intermédiaires. Les besoins de ces deux clientèles ne sont pas les mêmes et le milieux de vie que nous leur offrons se doit d'être adapté. »
“We define it now as longer than a 2 week stay”
“Sometimes when patients are in our PICU; their length of stay is " extra long"; but they no longer fit PICU criteria in any parameters and it is just sometimes " easier " to keep them until their issues are resolved.”
Some patients are acutely critically ill for long periods of time. This is different from a patient who is stable but technology dependent.

Appendix D

Survival Analysis

Survival analysis addresses empirical problems where the outcome variable of interest is time until an event occurs (Kleinbaum & Klein, 2012). For example, in the application to this thesis, each patients’ LOS will be the amount of time that expires before the “event”, which is the patient being discharged from the hospital. Generally, the time variable is referred to as “survival time” while the event is referred to as “failure”.

Often, issues can arise in these types of "time-to-event" problems where the event is not observed either because of study limitations (censoring) or other mutually exclusive events occurring (competing risks). While this is generally an important aspect of survival analysis, the only concern regarding censoring or competing risk for this thesis comes from patients whose stays ended in death rather than discharge from the PICU. However, the dataset underlying this thesis observes only 12 out 523 cases that ended in death. Since such issue will small role in this thesis, a more in-depth description of such problems can be found elsewhere (ie. Kleinbaum & Klein, 2012).

Hence, overlooking the problem of censoring, survival analysis is used in a scenario in which for each observation there is a distinct survival time, just as each patient has a defined LOS. Such information for any given population can be used to derive a survivor function, which demonstrates the probability of the event having occurred given a particular time. In the context of the PICU, the survivor function would show for any given time, the probability that a patient will still be in the PICU. Theoretically, this would be represented by some function:

$$S(t) = P(T \geq t)$$

where T is the event time, and t is some specified time. The function would start at 1 (no one has the event at time zero) and strictly decreases over time until it reaches 0, at the point at which all those under study have received the event. In practice, the function is obtained by plotting a step function using the survival times of those under study which may or may not start and end at zero depending on the data.

The hazard function *h(t)* gives the instantaneous potential per unit of time for the event (ie. discharge) to occur given that the individual has survived up to time *t*. More formally:

$$h(t) = \lim_{\Delta t \to 0} \left(\frac{P(t \leq T < t + \Delta t | T \geq t)}{\Delta t} \right)$$

Note, the hazard function estimates an instantaneous rate. It is a rate in that it is the probability of failure *over* an interval of time. It is instantaneous in that this interval approaches 0. In contrast to the survivor function which shows the probability of not failing (ie. staying in the PICU up to a certain time), the hazard function examines the probability of failure at a given point in time. These two core elements of survival analysis can be used in a regression framework to analyze the impact of different variables on the time to event variable in a variety of different ways. This facilitates the goal of this chapter to identify the effects of different covariates of LOS. Two such methods will be examined below: the semi-parametric Cox proportional hazard model (the most popular method), and the parametric accelerated failure time model (the method used for this thesis).

<u>Cox Proportional Hazard Model (Semiparametric)</u>

The most common method of regression in the survival framework is the Cox proportional hazards (PH) model. This method defines the hazard rate of an individual as a function of the time and a set of other explanatory variables. It assumes that each individual has an identical "baseline hazard function" which is modified by a set of *p* explanatory variables (**X**) as follows:

$$h(t, \boldsymbol{X}) = h_0(t) e^{\sum_{i=1}^{p} \beta_i X_i}$$

The parameters (β's) are estimate by maximizing the likelihood function (the joint probability of observing the data as a function of the parameters). From here, a hazard ratio can be defined which compares the h(t,**X**) of two individuals based on their covariates (**X**'s). Note that since both individuals are assumed to have the same baseline hazard function, it cancels out in the ratio and does not effect the result.

$$\widehat{HR} = \frac{h(t, \boldsymbol{X}^*)}{h(t, \boldsymbol{X})} = e^{\sum_{i=1}^{p} \beta_i (\boldsymbol{X}_i^* - \boldsymbol{X}_i)}$$

This estimate has the interpretation of an odds ratio: an individual with the covariates $\mathbf{X}^*$ is $\widehat{HR}$ times more likely to receive the event at any given time that an individual with the covariates **X**.

To understand the usefulness of this method in assessing the impact of different variables on LOS, consider an example. Consider a (0,1) variable that takes on a value of 1 if the patient is one-year-old or younger. The impact of this variable has on one's hazard ratio (β) is found using maximum likelihood estimation to be -0.5. Therefore:

$$\widehat{HR} = e^{\sum_{i=1}^{p} \beta_i (\boldsymbol{X}_i^* - \boldsymbol{X}_i)} = e^{-0.5(1-0)} = 0.61$$

In other words, and individual who is one-year-old or younger is 0.61 times more likely to be discharged from the hospital at any given time than an older individual. Reversed, an individual older than one is 1.64 times more likely to be discharged from the hospital at any given time then their younger counterparts.

One key assumption of the Cox model is that the baseline hazard function is constant across the groups or individuals being compared. In other words, the hazard ratio must be the same *at any given time*. In the example above, this means that patients one-year-old or younger must be 0.61 times more likely to fail at t=1 and t=20.

One of the key advantages of the Cox model is its semiparametric nature, it is not necessary to define an underlying hazard function. It is considered a "robust" model, in that it will closely approximate the correct parameterization without risking the wrong parameterization (Kleinbaum & Klein, 2012). Additionally, hazard ratios can be an easy to interpret measure of the effect of variables of interest. Finally, the Cox model has been observed to be less robust to unobserved heterogeneity then the parameterized AFT model explored below (Keiding, Andersen, & Klein, 1997).

Accelerated Failure Time Model (Parametric)

Parametric survival models assume that survival times follow a specific, known distribution. Unlike the semi-parametric model above, with the right parameterization, parametric models can completely specify the underlying hazard and survivor functions. While approximations of both functions can be obtained from semi-parametric models, the results from parametric models are simpler and more theoretically sound since both hazard and survivor functions can be expressed in terms of the probability density function that has been specified. However, the researcher risks specifying the *wrong* parameters. Notably, both accelerated failure time (AFT) and Cox models can be either parametric or semi-parametric. Therefore, it is important to note that it is specifically a parametric AFT and semi-parametric Cox model being treated in these two sections.

Examples of commonly used distributions include Weibull, exponential, log-logistic or lognormal distributions. For example, a Weibull distribution assumes:

$$h(t) = \theta p t^{p-1}$$

$$S(t) = \exp(-\theta t^{p})$$

$$f(t) = \theta p t^{p-1} \exp(-\theta t^{p})$$

Whereas a log-logistic distribution assumes:

$$h(t) = \frac{\theta^p p t^{p-1}}{[(1 + (\theta t)^p)]}$$

$$S(t) = \frac{1}{[(1 + (\theta t)^p)]}$$

Where f(t) is the probability density function, p is a shape parameter and θ is a scale parameter. As noted above, specifying the parameters of one of the functions above implies the other two.

AFT models assume the covariates of interest have a multiplicative effect on *survival* time, contrary to proportional hazard models which assume a multiplicative effect on the *hazard*. The result is predictor variables causing a "stretching out" or contraction of survival time. An individual's survival function would be represented as follows:

$$S(t) = S_0(\theta t)$$

Where $S_0(.)$ is the assumed parametrization and θ represents the effect of covariates on survival time.

To understand further, consider the case of dogs being said to age 7 times faster than humans. In this case a dog would survive past 1 year with the same probability as a human surviving past 7 years, and similarly the survival of a 10-year-old dog would be equivalent to a 70-year-old human. If one were to assume a Weibull distribution, the survival function of any given "individual" (dog or human) would be:

$$S(t) = \exp(-7^x t^p)$$

Where x takes on a value of 1 for humans and 0 for dogs. Evidently, the probability and dog will be alive at any time *t* is the same as the probability a human will be alive at time 7*t*.

Hence, the parameter θ, or the acceleration factor, is the key measure of the effect of covariates on survival time. The coefficient on each variable that determines θ is estimated using maximum likelihood estimation. The parameter θ has the interpretation of being a ratio of survival times corresponding to a fixed value of S(t). In other words, in the case of single a 0,1 variable, it will take an individual in group 1 θ times longer to reach 75% probability of survival, 25% probability of survival, or any other given survival value. Additionally, there is the benefit of being able to directly interpret the coefficients as semi-elasticities in Weibull and exponential distributions.

To understand all this more explicitly, consider an AFT model parameterized with a Weibull distribution modeling the same impact of a binary age variable on LOS as described in the Cox PH model above.

$$S_i(t) = \exp(-e^{1.2+0.63x_i}t^{0.85})$$

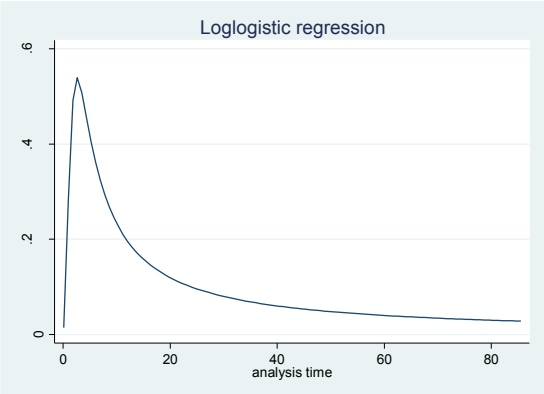
Consider the case where t=10. For those one years-old or younger S(t)=0.32 while for older patients S(t)=0.12. In other words, 88% of older patients will have been discharged after 10 days in the PICU, while only 68% will be discharged after the same amount of time. Additionally, in the Weibull distribution, the coefficient can be interpreted as a semi-elasticity. In other words, younger patients have 88% ($e^{0.63}$-1) longer stays than older patients on average. Notably, $e^{\alpha}-1 \approx \alpha$ for lower values of α.

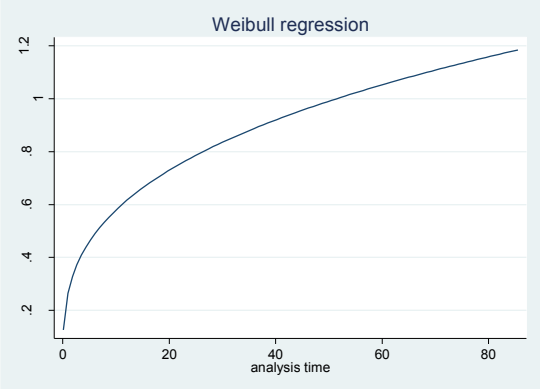
One key assumption of the AFT model is the AFT assumption, that the effect of covariates is proportional with respect to survival time. In other words, the acceleration

factor between two groups or individuals must be true at all times. Returning to the human/dog example, the acceleration factor is constant at 7: 1-year-old dog=7-year-old human and 10-year-old dog=70-year-old human. Note that covariates are proportional to *survival time*, rather than proportional to the hazard, as in the PH assumption. Notably, for Weibull distributions (and only this distribution) if the AFT assumption holds then the PH assumption holds, and vice versa.

One of the advantages of the AFT model over the Cox model is the reliance on the AFT assumption rather than the PH assumption. Depending on the relationship between the covariates and the outcome this may be a more appropriate assumption. While hazard ratios are well established in the literature, the direct impact on survival time and the interpretation of the coefficients as semi-elasticities may make the output of the AFT model easier to interpret. Additionally, the correct parametric specification is preferred to a semiparametric one, however the researcher risks mis-specifying the model. Finally, this model has been shown to be more robust to unobserved heterogeneity then Cox model explored above (Keiding, Andersen, & Klein, 1997).

Appendix E

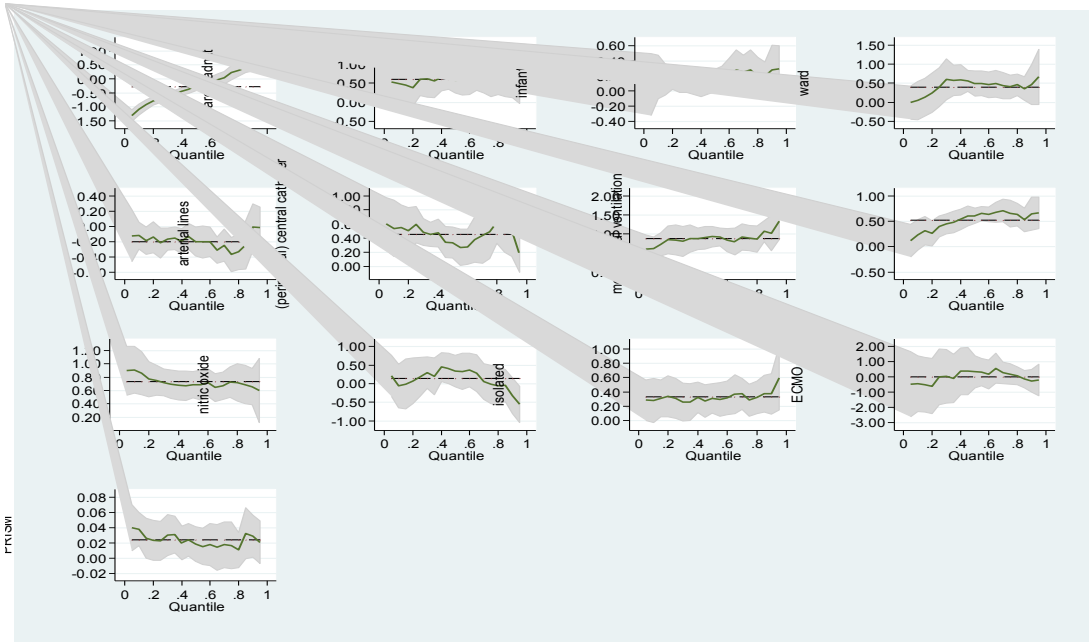




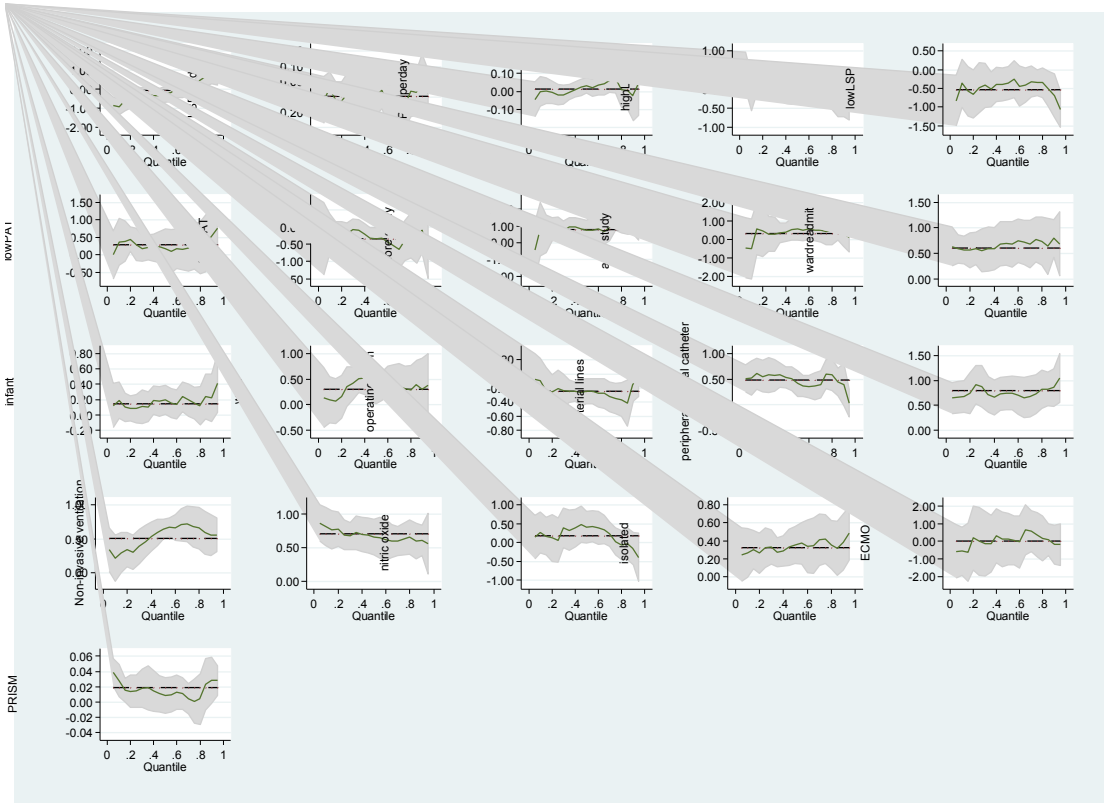
Appendix F

Variable	**Reason**
Season	No discernable effect
Previous stays	No discernable effect
Age (other than infant)	No discernable effect
Month of admission	No theoretical basis
Time of admission (hour)	No theoretical basis
Nitric oxide during admission (and other technology)	No effect with controls
Cardiac surgery (and other "types")	No effect with controls
Other hospital (and other "admit from")	No effect with controls
Other LSPs/Patients per day (see chapter 3)	Unknown before stay
Many/few other patients per day	Unknown before stay
Patient discharged and readmit within 48 hours between recorded admit and discharge times	Unknown before stay

Appendix G



Appendix H



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