Implementation Strategies used to Reduce Unplanned Extubations (UPE) in the Neonatal Intensive Care Unit at The Hospital for Sick Children (SickKids)

by

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An oral defense of this thesis took place on August 30, 2021 in front of the following examining committee:

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Chair of Examining Committee	Dr. Meghann Lloyd
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The above committee determined that the thesis is acceptable in form and content and that a satisfactory knowledge of the field covered by the thesis was demonstrated by the candidate during an oral examination. A signed copy of the Certificate of Approval is available from the School of Graduate and Postdoctoral Studies.

ABSTRACT

This study analyzed unplanned extubation (UPE) reduction strategies as well as patient characteristics and other risk factors for all UPEs that occurred between January 1, 2007 and December 31, 2019 in the neonatal intensive care unit (NICU) at the Hospital for Sick Children (SickKids) in Toronto, Canada. Six major implementation strategies decreased UPEs per 100 ventilator days from 2.38 to 0.45 between 2003 and 2019. The study sample included 302 UPEs (252 infants) with 12% infants with repeated UPEs. The study analyzed the association of NICU UPEs with previous UPE history, birth weight, gestational age, taping protocol, procedures prior to UPE, sedation concern, patient restraint, type of endotracheal tube, loose tape, length of mechanical ventilation and length of NICU stay. These findings would be helpful for other healthcare facilities and researchers to inform the development of UPE reduction frameworks, and to improve patient outcomes.

Keywords: mechanical ventilation; unplanned extubation; neonatal intensive care unit (NICU); UPE reduction strategies; UPE risk factors

AUTHOR'S DECLARATION

I hereby declare that this thesis consists of original work of which I have authored. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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The research work in this thesis that was performed in compliance with the regulations of Research Ethics Board/Animal Care Committee under REB Certificate number 16110 (Ontario Tech University) and 1000066879 (Hospital for Sick Children).

________________________________ Samira Ansari

STATEMENT OF CONTRIBUTIONS

I hereby certify that I am the sole author of this thesis and that no part of this thesis has been published or submitted for publication. I have used standard referencing practices to acknowledge ideas, research techniques, or other materials that belong to others. Furthermore, I hereby certify that I am the sole source of the creative works and/or inventive knowledge described in this thesis.

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LIST OF ABBREVIATIONS AND SYMBOLS

ACTS	Acute Care Transport Services
aOR	adjusted Odds Ratio
BW	Birth Weight
CA	Chronological Age
CI	Confidence Interval
CIHI	Canadian Institute of Health Information
CQI	Continuous Quality Improvement
ETT	Endotracheal Tube
GA	Gestational Age
IQR	Interquartile Range
LOS	Length of Stay
MV	Mechanical Ventilation
NICU	Neonatal Intensive Care Unit
OR	Odds Ratio
PDSA	Plan-Do-Study-Act
PICU	Pediatric Intensive Care Unit
PMA	Postmenstrual Age
QI	Quality Improvement
RDS	Respiratory Distress Syndrome
RR	Risk Ratio
RUE	Reduce Unplanned Extubation
SickKids	The Hospital for Sick Children
UPE	Unplanned Extubation
VLBW	Very Low Birth Weight

Chapter 1. Introduction

1.1 Background

Infants or neonates, are admitted to neonatal intensive care units (NICUs) when specialized care is needed. Most neonates admitted to the NICU are preterm (born before 37 weeks of pregnancy), have low birth weight (< 2500 grams or < 5.5 pounds), or have a health condition that needs special care such as Respiratory Distress Syndrome (RDS), sepsis or infection, hypoglycemia, maternal chorioamnionitis, congenital anomalies or birth defects, seizures, or severe intra uterine birth restriction etc. Each year around 15 million babies are born preterm which translates to more than 1 in every 10 babies (1). According to the Canadian Institute of Health Information (CIHI) 14.4% of the newborns born in 2001-2002 in Canada (excluding Quebec, rural Manitoba and the Territories) were admitted to a NICU (2). Compared with the rate of 12.6% in 1994-95, the number of NICU admissions were increased by approximately 1,500 (2). The median length of stay (LOS) in a NICU was two days for low-birth-weight babies and 23 days for very-low-birth-weight babies (Canadian Institute for Health Information, 2004). A 2021 study (2) that took place between 2006-07 and 2008-09, showed 11.1% of newborns were admitted to NICU, with the highest rate in New Brunswick (24.5%) and the lowest in Quebec (5.3%). As neonates in NICU are admitted for specialized care, any adverse event could pose significant health risks for them.

Mechanical ventilation (MV) is a life supporting treatment to help patients when they are unable to breathe by themselves. In most cases the process is used to support patients with respiratory, neurological, and cardiac failure (3-8). MV delivers positive pressure in order to take over or regulate an individual’s breathing through an open airway such as an endotracheal tube (ETT) (9-12).

Extubations are considered successful when weaning and removal of the ETT from MV are performed as per the medical team’s plan. Unplanned extubation (UPE) on the other hand, is the premature or unintended removal of an artificial airway (ETT, tracheostomy tube) by the patient, caregiver or staff (13, 14). UPEs are often associated with infant agitation (including head turning), suctioning, loose tapes, ETT taping or re-taping, length of tube too short between the lip and the ETT adapter, and procedures (weighing, bathing) (15).

The incidence rate of UPEs is highly variable. In adults it ranges between 3.4% to 22.5% (16). For children up to 17 years, the average rate in the pediatric intensive care unit (PICU) is 8% (varies from 0.8% to 18.5%). In neonates, across different studies the rate varied between 1% and 80.8% (with a median of 18.2%) in neonatal intensive care unit (NICU), or from 0.14 to 5.3 UPEs/100 ventilator days (17).

UPEs can cause serious adverse events, including hemodynamic instability, increased sepsis risk, increased duration of MV and NICU LOS, and complications from re-intubation (higher risk for cardiopulmonary resuscitation, tracheostomy, death) (14, 17, 18). In the USA, 14,000 UPE occur in NICU yearly, and the health care costs of both the PICU and NICU UPEs is over $500 million (19). In 2002–2003, the average cost for Canadian hospitals per NICU admission was $9,700 (20). For the same time horizon, the average cost per newborn stay was $795 for babies of normal birth weight (BW) delivered vaginally without a NICU admission (20).A study conducted by Rios et. al. (2021) (21) estimated the NICU admission cost for 27,742 infants with preterm birth from 30 tertiary NICUs in Canada. The median (IQR) inpatient hospitalization cost was $20,184 ($9,739-51,314); among them for infants born at gestational age 33-36 weeks, the cost was $11,810 ($6,410-19,800); at 29- 32 weeks, $30,572 ($16,597-$51,857); and below 29 weeks, $100,440 ($56,858-$159,3867). If we consider data (22) from 2019-20 where a total of 363,943 newborns were born in hospital, and an average NICU admission rate of 11.1% (2), there would be approximately 41,000 infants admitted to NICU each year. Finally, approximately 7,600 UPEs in NICUs may occur in Canada, considering a median 18.2% NICU UPE occurrence rate {da Silva, 2013 #14). The average cost of UPEs in NICU, or additional NICU stay due to UPEs, are not readily available for Canada. However, considering the average cost of $20,184 for a NICU admission and 7,600 UPEs in NICU, the total annual cost for NICU UPE events could be significant. Looking at the clinical magnitude and the economic cost of UPE events, it is important to identify the issues that cause UPEs as well as understand how UPE events can be reduced.

1.2 Need for Implementation Strategies to Reduce UPEs

The Society for Airway Management and the Patient Safety Movement Foundation is a coalition of a multi-disciplinary group of medical societies, patient safety and quality improvement (QI) organizations, including (a) medical professional societies such as American Academy of Pediatrics, American Associations of Nurse Anesthetists, American Association of Respiratory Care, American College of Emergency Physicians, Society for Airway management, Society of Critical Care Medicine, Society for Pediatric Anesthesia, National Association of Neonatal Nurses, National Association of EMS Physicians; (b) patient safety organization organizations like Airway Safety Movement, Do it for Drew Foundation, Patient Safety Movement Foundation, Children's Hospital's Solution for Patient Safety; and (c) QI organizations like IMPAQ/ Centers for Medicare and Medicaid Services Strategic Innovation Engine. This organization has members from different countries around the world, and the mandate is to reduce the incidence of UPE, and thus prevent harm and death (23). In order to do this they recommend hospitals take the following three actions (23):

1. Take inventory and do an assessment to determine the hospital's rate of UPE. This will help set targets for improvement.
2. Collaborate with the local quality and safety teams to increase awareness of UPE and provide the resources for QI initiatives.
3. Develop a QI Initiative.

The Hospital for Sick Children (SickKids) NICU in Toronto has undertaken all three of the Society for Airway Management and the Patient Safety Movement Foundation actions since 2007. In 2007 the SickKids NICU started using NeoBar, an endotracheal tube stabilization device, to help reduce UPE. This strategy did not significantly impact the UPE rate, thus in 2008 a "Reduce Unplanned Extubation" (RUE) team was developed, spearheaded by respiratory therapists (RTs). It consisted of an interprofessional team that included RT, nursing, medicine, quality & safety, the Acute Care Transport Services (ACTS), caregivers, and systems analysts. Its purpose was to evaluate baseline data and develop QI interventions to help reduce the rate of UPE in the NICU by 50% using the "Plan-Do-Study-Act" (PDSA) cycle (24). Since 2008 the RUE team has completed 5 PDSA cycles that included multiple and standardized strategies. They have reduced their

UPE rate well beyond the 50% from 3.0 to 0.2 per 100 ventilator days and continue to strive for lower and lower numbers with each PDSA cycle. However, up to now, the methods and strategies used, and their influence on the reduction has not been analyzed to assess the impact of the QI interventions individually and interrelatedly.

1.3 Purpose of the Study and Research Questions

The NICU RUE team at SickKids has achieved success at reducing UPE rates between 2007 and 2019. The purpose of this study is to describe the methods and strategies used by the NIUC RUE team that resulted in reducing UPE rates at SickKids. These methods and strategies could be generalizable and enable other neonatal health care institutions to standardize their UPE reductions strategies (and other QI interventions) using a similar framework.

1. Describe the implementation strategies used to reduce UPE in the SickKids NICU, and their influence on UPE rates in the SickKids NICU.
2. Describe contributing factors and patient characteristics of infants who had a UPE, and compare them between biological sex (since no literature was found comparing UPE characteristics between biological sex). We hypothesized that male infants experience a higher number of UPEs, and worse outcomes, compared to female infants.

1.4 Research Significance

The impacts or effectiveness of implementation strategies to reduce UPEs vary largely across existing studies. This research will describe the SickKids NICU implementation strategies and their impacts on UPE rate. This will inform the development of an implementation framework that could be used for future NICU research and other various clinical practices. It will help guide researchers and clinicians when implementing new strategies in the NICU, potentially improving patient outcomes.

1.5 Ethical Considerations

This study was approved by the research ethics boards of SickKids (#1000066879), and Ontario Tech University (#16110). Approval letters can be found in Appendix 1.

1.6 Thesis Format

This thesis is organized into four chapters. Chapter 1 provides a background on UPEs, research significance and research objectives. Chapter 2 provides a literature review on factors associated with UPE events, and various implementation strategies that have been used to reduce UPEs. Chapter 3 describes the research manuscript including background, methodology, results and conclusions. Finally, Chapter 4 provides overall conclusions and next steps.

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Chapter 2. Literature Review

2.1 Search Strategy

To meet the objectives of the study, and with the help of the SickKids librarian (Quenby Mahood), the following topics were searched and included: incidence of UPEs in NICUs, risk factors associated with UPEs, and implementation strategies used to reduce UPEs. Appendix C details the databases searched (Medline, Embase, Central), and number of results (n=450), since inception until April 2020. In addition, 98 records were identified in the PubMed database when the reference lists of studies related to neonatal UPEs were searched. After removal of the duplicates, 368 studies remained. The following studies were then selected and described in this literature review: (a) English language, (2) UPE events occurred in the NICU, (3) described risk factors associated with UPEs, (4) identified causes of UPEs, (5) described common UPE reduction implementation strategies (including QI), and (6) reviewed effectiveness of implementation strategies (a total of 92 studies). Figure 1 provides details on the search strategy flow for this study. This literature review will describe UPE implementation strategies and outcomes, and risk factors associated with UPEs.

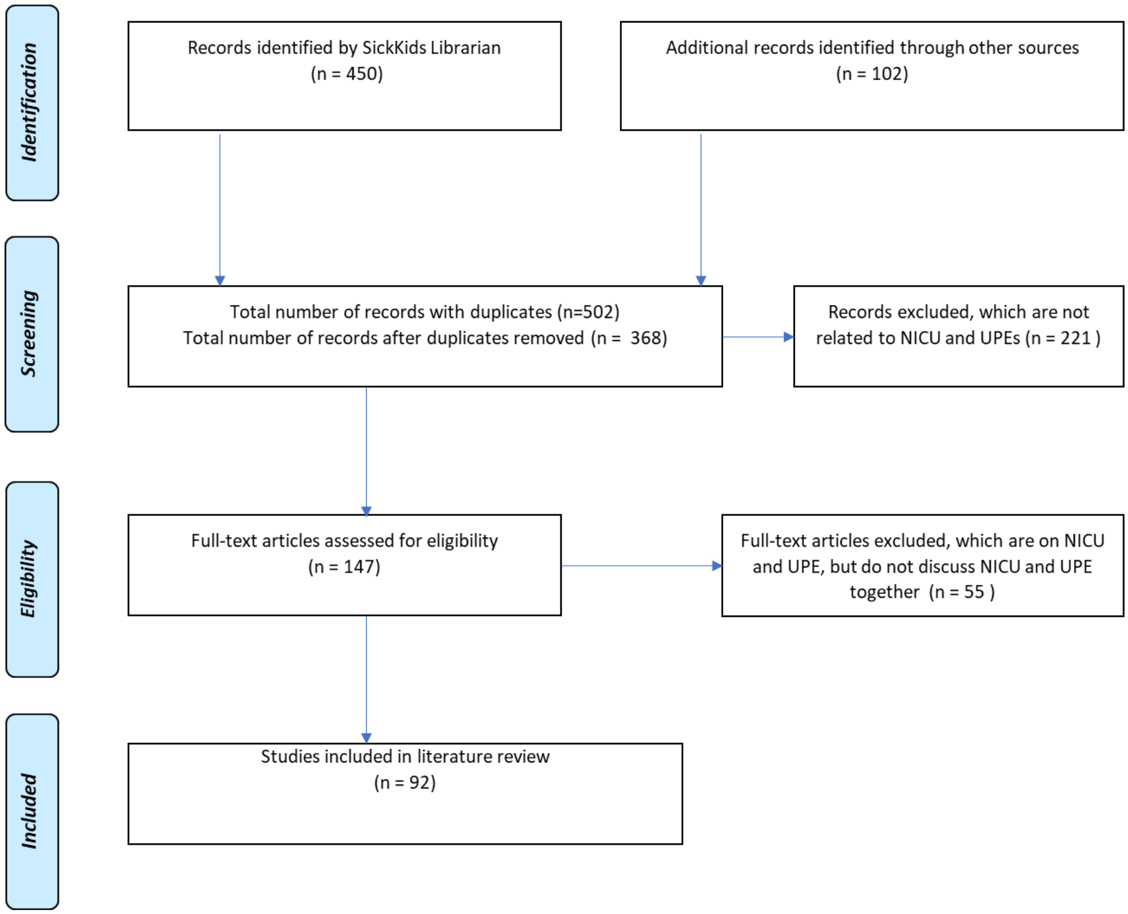

Figure 1 PRISMA(1) flow diagram of literature search

In this study, no established literature review framework was followed. Hilary and Lisa (2005) (2) identified some forms of literature review such as systematic review, scoping review, narrative review, structured review, and research synthesis. The authors acknowledged no literature review type is ideal and should be selected based on the researchers needs. However, the authors found scoping review as the most widely used literature review method. Scoping review aims to map the key concepts of a research area and address broader topics where many different study designs might be applicable (3). The literature review of this study has a lot of similarities with scoping review method. At first the research area was divided into two groups and later each group was divided into several categories e.g. for literature on UPE reduction strategies we provided a description for each type of strategy. This thesis literature review consisted a fair number of peer-reviewed studies, using standard keywords for NICU UPE. The literature search was completed by an experienced health librarian at SickKids, in well-known electronic databases. However, some limitations were also observed when the literature review was conducted including: a) lack of studies with longer duration; b) studies with small sample size; c) missing information due to poor documentation; d) inconsistent conclusions; and e) less NICU UPE studies compared to adult UPE studies. Given there was no sensitivity analyses done based on methodological quality, the conclusions drawn from our literature review are also influenced by these limitations.

2.2 UPE Implementation strategies and outcomes

Implementation science is defined as "the scientific study of methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice, and, hence, to improve the quality and effectiveness of health services" Eccles and Mittman (4). It acts as a bridge between researchers and health service providers, sociologists, economists, front-line clinicians etc. (5) The scope of implementation science includes patients, health care service providers, organizations and policy makers. It considers trans-disciplinary research teams, and includes both qualitative and quantitative methods. (6) Implementation strategies involve integrated bundles of discrete methods or techniques to address specific issues (5). Once a healthcare issue is identified, different types of strategies can be implemented, and the success and failures of the strategies can be evaluated. Analyzing implementation strategies and documenting its effectiveness can play a critical role in improving the healthcare system.

2.2.1 Endotracheal tube (ETT) Management Strategies

There are many examples of UPE-specific implementation focused studies that identify issues, implement strategies, and evaluate effectiveness. Some involve simple changes such as taping procedures and/or brand (7-10), while others include multiple strategies such as protocols, bundles or checklists(11). Loughead et al. (2008) (12) conducted a retrospective cohort review in Central Dupage Hospital in Wheaton, Illinois. They reviewed medical records of all hospitalized infants who received MV between 2002 and 2007, to understand factors associated with NICU UPEs as well as to modify the current practice to reduce UPEs. An interdisciplinary team was formed, and continuous data were collected. The study identified patient activity, caregiver activity, and loose tape as the top three causes of UPE. To reduce UPEs the medical team implemented two strategies: consistent taping techniques, and umbilical clamping the ETT. They observed overall reduction of UPE rates, from 4.8 to 0.9 UPEs/100 ventilator days over a period of 5.5 years (January 2002- June 2007). The study recommended setting goals and targets, providing proper education for caregivers, and continuously monitoring real-time data in order to reduce UPEs.

Barrosse et al. (2019) (13) developed and implemented strategies to standardize ETT management processes in order to reduce UPEs in the NICU. As the UPE events mostly occurred during chest x-ray of infants, the study implemented a “holding the ETT during an x-ray” strategy. A goal to achieve between 48% and 70% “holding the ETT during an x-ray” incidences was set. In order to attain the target, strategies included daily ETT audits, decreasing ETT manipulations, increasing education and awareness, and co-ordinating multidisciplinary care. The strategies were successful as the “holding the ETT during an x-ray” incidences increased from 48% to 91% in a four-month period between October 2018 and February 2019. The study also observed increased awareness among staffs, showing an increase (79% to 100%) in documenting location of ETT during x-ray.

2.2.2 Evidence-Based Strategies

Hu et al. (2017) (11) conducted a study to implement evidence-based practice and assess the impact of the strategies in reducing UPEs in the NICU. They implemented three-phased standardized evidence-based strategies that included stakeholder engagement, implementation of best practice (compliance for standard care documentation, compliance for standard care implementation, and compliance for staff education), and follow-up. They found a reduction in UPE rates from 2.3 to 0.36 per 100 ventilator days, and increased compliance in procedures and documentation around ETT security. Similarly, Crezee et al. (2017)(14) conducted a study to observe the effectiveness multi-step strategies including: 1) at least two care providers at the bedside for the movement of intubated patients 2) standardizing head and ETT position, 3) establishing a set methodology for ETT security, (4) improved post operative communication, and 5) a post-UPE assessment tool. This resulted in a 50% decrease in monthly UPE events (from

3.8 to 1.9 per month). The UPE events per 100 ventilator days before implementation decreased by 53% (from 1.15 to 0.54) (January to December 2013) compared with after implementation (January to December 2014).

2.2.3 Staff Education Strategies

Hewitt et al. (15) conducted a QI study to examine the effectiveness of an education-based QI initiative aimed at all NICU staffs to decrease UPE rate in the NICU. The study calculated UPE rates and identified risk factors using a retrospective chart review. Later a QI program was implemented and included multi-disciplinary NICU staff education session, placement of education posters in the NICU, and identification of high-risk neonates. After the six months of implementation, it was observed that the UPE rate decreased from 3.28 to 1.45 per 100 ventilations days. It was also observed that rate of re-intubation following an UPE event decreased from 78.3% to 50%. There are several examples of other staff education strategies to reduce UPEs, found within comprehensive QI initiatives utilizing “plan-do-study-act” (PDSA) cycles (and described below).

2.2.4 Plan-Do-Study-Act Strategies

Sadowski et al. (2004) (16) conducted a study focusing on a continuous QI (CQI) strategy to reduce UPEs. A multidisciplinary CQI team was developed and a PDSA strategy was implemented. The phase 1 (“plan”) included quantification and benchmarking of UPEs as well as identifying the factors causing UPEs (using a five-year retrospective review of demographic and clinical information on neonates that required MV). The phase 2 (“do”) included implementation of the education program and designing a protocol for weaning. The phase 3 (“study”) included evaluation of the data trend, and the phase 4 (“act”) included evaluation of the strategies and sharing the results with clinical providers. Through the four staged PDSA cycle between 1996 and 2001, the study showed significant decreases in UPEs rates, from 1.5 to 0.8 UPEs per 100 ventilation days. Patient characteristics may have contributed to the reduction in UPEs, but were not accounted for in their analyses. The authors suggested to monitor and consider other factors while evaluating the success of any implementation strategies.

The PDSA cycle strategy was also used by Fontánez-Nieves et al. (2016) (8) in a study that targeted a reduction of 50% in UPEs. Loose tape was identified as one of the important factors behind UPEs. Strategies to secure ETT were created (“plan”). During the study various types of ETT securing methods were implemented (”do”) and evaluated (“study”) to achieve the optimal ETT securing method. This study also implemented an ETT securing method training program for all nursing staffs followed by hands-on training session and workshop. The nurses were required to document ETT settings in the central computerized system for continuous monitoring. These strategies resulted in 72% decrease in UPE rate (16.1 to 4.5 UPEs per 100 ventilation days) between 2012 and 2014.

Powell et al. (2016) (10) conducted a study using a rapid-cycle PDSA cycle method. First a survey was conducted among nurses and respiratory therapists to identify the causes and impacts of UPEs on care. Based on the survey results, strategies were implemented in two phases. The phase 1 standardized the process for turning intubated infants, assessing ETT placement, and communicating tube position with caregivers. Phase 2 addressed respiratory plans of care, correcting ETT migration, establishing ETT re-securement methods, and standardizing position during radiography. UPE rate decreased from 3.8 to 2.7 per 100 ventilation days due to the strategies in four months while each phase lasted for 2 months. The study also observed a reduction in number of ventilator days ($p<0.001$) between pre and post improvement phases. Invasive MV cases reduced from 1,700 to 400 ventilator days and non-invasive MV cases from 1,300 to 600 ventilator days.

Igo et al. (2021) (17) completed a QI project using a PDSA cycle to reduce UPEs and associated morbidities in a level 4 NICU facility. At baseline (March to November 2017) the UPE rate was 9.9 per 100 ventilator days. The UPE reduction strategies included creation of an inter-professional task force, consistent reporting and documentation, increasing staff awareness by providing UPE details to the unit “huddle” board, intense staff training for ETT securement, two-person care for transferring intubated infants, placement of mittens for >34 weeks GA infants, and daily re-taping of the ETT device. The RTs also provided 1:1 hand-on instruction on ETT placement and maintenance. The results showed a significant 84% reduction, from a mean 9.9 to 1.6 UPEs per 100 ventilator days (for the period between August 2018 and March 2019).

2.2.5 Strategies without success

While many studies observed success in reducing UPE rates because of the implementation strategies, some studies found little impact on UPE rates after implementing strategies. Loganathan et al. (9) compared the use of an ETT stabilization device (NeoBar®) on UPE rate, and observed a 20% decrease, from 1.47 to 1.17 per 100 ventilation days, though the reduction was not statistically significant (p=0.91). This result was likely confounded by gestational age (GA) and BW, as they were both lower for the post-implementation group. The author suggested to control for potential confounding factors before evaluating the success of any implementation strategy.

Ferraz et al. (2019) (7) evaluated a 16-month UPE bundle that included a new ETT fixation model, team training, identification of neonates at risk of UPE, and debriefing after UPE episodes. The authors observed higher BW and daytime period were associated with lower risk of UPEs. They found a reduction in UPEs, from 19.9% to 14.6%, in newborn infants because of the implementation. However, the reduction was not statistically significant potentially because 34% of infants in the study sample were of very low birth weight (VLBW).

Utrera et al. (2014) (18) conducted a two staged implementation strategy study. The first phase involved calculation of UPE rates and understanding the causes of UPEs. The second phase consisted of training of nurses, and ETT fixation methods. They observed no significant reduction in UPE rates. In the first and second stage, the UPE rates were 5 and 4.5 per 100 ventilations days respectively. In both stages, UPEs occurred during patient handling, and the re-intubation incidence was 77.7% (stage 1) and 67.4% (stage 2) respectively. The authors observed higher UPE rate of 6.2 per 100 ventilations days (combining stage 1 and 2) during summer months of July, August and September, compared to other months of the year. The reason behind the increased UPE rates during summer was possibly attributed to the recruitment of less experienced nurses during summer months.(18)

Ligi et al. (2010) (19) conducted a study for a period of two years to see the impact of continuous incidence monitoring and subsequent prevention strategies (such as hand-washing educational program, efforts to minimize use of invasive devices, guidance for insertion and maintenance of central catheters, guidance for enteral feeding and use of using catheters for extremely low-birth weight neonates, guidance for ETT placement during every position change, and suction procedure for neonates). While these strategies achieved improvement in iatrogenic events, infection due to catheter, and drug-dosing errors, there was a significant *increase* in UPE events from 5.6 to 15.5 UPEs per 100 ventilation days. The author identified four potential causes: (i) ETT became dislodged during spontaneous movement, (ii) hospital policy change eliminating use of tincture of benzoin which usually help to adhere the tube with skin (iii) reduced use of bilateral Y-strip tape, and (iv) high turnover of caregivers during the study period. The authors speculated that continuous incidence monitoring could achieve success when it is followed by preventive strategies to improve quality care and patient safety.

2.3 UPEs and Risk Factors

Several studies and QI initiatives have investigated the importance of developing strategies to reduce UPE rates and improve patient safety in the NICU. Before techniques and strategies to reduce UPEs are developed, understanding the association between risk factors and UPE events is necessary.

da Silva et al. (2013) (20) completed a systematic review on existing literatures between January 1950 and January 2012 to understand the current knowledge of UPEs and their risk factors in NICUs. This study had a rigorous study design and included many relevant studies on neonatal UPEs. The authors identified 192 studies for detailed review, and 15 studies were considered for the final synthesis. It included 11 prospective cohort studies (19, 21-30), three retrospective cohort studies (31-33), and one retrospective and prospective cohort study (12). Based on the literatures, the authors observed UPE rates (between 1977 and 2010) ranging from 0.14 UPEs/100 ventilation days (32) to 5.3 UPEs/100 ventilation days (29). This rate was similar when considering only recent literatures (between 2005 and 2010) with UPE rates varying between 0.56 UPEs/ 100 ventilator days (19) and 5.3 UPEs/100 ventilator days (29). This study looked at many different types of UPE risk factors, immediate outcomes of UPEs, and preventive measures to reduce UPEs. Risk factors assessed and reported in the studies included agitation, ETT manipulation, loose or wet tape, prolonged mechanical ventilation (MV), kangaroo-care (skin-to-skin contact), GA, lack of physical restraint, previous UPE events, self-extubation, weaning stage, and nurse-patient ratio. Among these factors, the first six factors were reported in 75% of all studies.

Sections 2.3.1 to 2.3.6 describe different risk factors, and are categorized according to the study objectives, and other data collected for this study.

2.3.1 Impacts of Sex

With respect to biological sex, a few studies have identified male associations with UPEs. Aydon et al. (2018) (34) conducted an audit to gather information on UPEs that took place in the NICU between August 2015 and February 2016. A total of 224 episodes of ventilation were found among which 41 had UPEs. Out of 224 episodes, 114 episodes were in male babies and 68 in female babies. Male babies had three times higher incidence than female babies, with 27% (31 out of 114) and 16% (11 out of 68) experiencing UPEs respectively. Similar findings were also observed by Razavi et al. (2013) (35) who conducted a retrospective cohort study comparing 59 patients who had a UPE in the PICU, with 180 matched controls. A multivariate regression analysis found the odds ratio (OR) for UPE in male babies was 2.53 (95% CI of 1.35-4.23, p=0.005) compared to 0.67 (95% CI of 0.55-1.48, p=0.71) for female babies. In contrast, a 2017 retrospective cohort study was conducted by Mhanna et al. (39) analyzed the demographics, prenatal characteristics and medication use of VLBW infants. During the study period of 2009-2012, 45 out of 147 infants (31%) experienced UPEs. This study did not find any statistical differences between UPE and non-UPE infants regarding biological sex, nor discussed why statically differences were not observed. A possible explanation for non-significance may have been the inconsistent care given to both male and female infants. Another possible explanation could be because of their very early age; hormonal influence was not very strong and therefore, the impact of biological sex not significantly observed.

2.3.2 Impacts of Gestation Age and Birth Weight

The influence of GA and BW risk factors on UPE rates were highly variable among the different studies. da Silva et al. (2013) (20) were not able to draw clear conclusions on whether the GA and postmenstrual age (PMA=GA + chronological age [CA]) significantly increased UPE risk. The authors identified one study (19) stating higher incidence of UPEs for infants with GA more than 34 weeks while two studies (28, 31) showed no association between GA and UPEs. Hatch et al. (2017)(36) published a study after the 2013 da Silva systematic review (20), using an 18-month prospective cohort study on critically ill newborns to describe the anatomical and developmental factors on the risk of UPE. A total of 718 infants were ventilated and 118 UPEs happened in 81 infants. The authors considered CA, PMA, and BW in their analyses. A multivariate regression model showed a non-linear relationship ($p < 0.01$) between CA and UPEs. The daily probability of UPE did not change significantly during the first 7 days of life (adjusted odds ratio [aOR]: 0.5, 95% confidence interval [CI]: 0.17–1.47). But after the first week of life, the daily probability of UPE increased over the remainder of the NICU stay period with the greatest increase between chronological day 7 and 28 (aOR: 1.36; 95% CI: 1.06–1.75). The study did not find any statistically significant impacts of PMA and BW on UPE events.

da Silva et al. (2013) (20) also observed inconsistent findings between BW and UPEs. Two studies conducted by Brown et al. (1998) (23) and Horimoto et al. (1991) (33), observed high UPEs for low BW infants. Brown et al. (1988) (23) found higher UPE rates for neonates below 1,500g compared to neonates over 1,500 g ($p<0.04$). Likewise, Horimoto et al. (1991) (33) found higher UPE rates (87%) for infants below 2,500 g. On the other hand, in da Silva et al. (2013) systematic review (20), three studies (24, 28, 31) showed no difference in BW between infants who had a UPE and a control group (i.e., non-UPE infants). One study (31) using a retrospective cohort design with preterm and newborn infants did not observe higher UPEs for lower BW and GA. The Mhanna et al. (2017) (37) retrospective cohort study (also published after the 2013 da Silva systematic review (20)) found the mean BW of UPE infants were 885 grams and the mean BW of non-UPE infants were 1,075 grams; lower BW infants had higher risk of UPE incidence ($p<0.01$). Similarly, the mean GA was less for the infants (mean GA 26.7 weeks) who experienced UPE and compared to non-UPE infants (mean GA 27.7 weeks, $p=0.01$). Note when practised health providers were assigned lower BW and GA infants, their prior infant handling experience may have resulted in less UPEs(31).

2.3.3 Procedures at the time of UPE

A few studies noted certain procedures were associated with UPEs in the NICU. In the systematic review by da Silva et al. (2013) (20), ETT manipulation (such as suctioning, re-taping, unsupported ventilator tubing) at the time of UPE ranged from 17% (27) to 30% (26) (median 26.5, IQR 21–29%). Fontanez-Nieves et al. (2016) (8) in a PDSA QI study, found 29% of UPEs (over a seven-month period) were associated with patient movement. Self-extubation was identified as a primary cause of UPEs with Franck et al. (1992) (26) reporting 62%, and Garrido et al. (2009) (38) reporting 73% of UPEs happened because of this reason. Balon, J. (2001) (39) conducted a study to identify the common factors behind “spontaneous” self-extubation in critical care unit (not specific to NICU), and found that physical restraints, reintubation, and localized painful stimuli were some of the common causes of self-extubation. Finally, weaning (at various stages) was commonly associated with UPEs with 44% (19) occurring in one study, and 76% (38) in another study.

2.3.4 Impacts of Sedation

The impacts of sedations on UPEs were analyzed in different studies, but those taking place in the NICU were limited. Sedation is an important factor as da Silva (2013) (20) systematic review included seven studies (12, 19, 23, 24, 28, 31) that found restlessness/agitation occurred betwen 13% (12) and 89% (19) of all infants who had

UPEs (median 25%, IQR 16.6–57.2%). Popernack et al. (2004) (40) conducted a prospective, observational study to determine how a standardized sedation algorithm impacted UPEs for PICU patients. The algorithm included six levels of sedation (Level 1 no sedation required, only analgesics for pain relief required; Level 6 continuous analgesics and continuous paralytics). After the implementation of the algorithm, the UPE rate decreased from 0.44-0.63 to 0-0.19 per 100 ventilator days ($p<0.001$). The authors noted that no other changes were made to the patient care system throughout the entire study period, increasing the likelihood that the effect on UPE was due to standardized sedation practices, and not other variables. In contrast, Dreyfus et al. (2017) (41) conducted a study in children between 0 and 18 years (who required MV for at least 24 hours between January 2013 and March 2015) to observe the impact of a sedation protocol on UPEs. No significant impact of the sedation protocol was observed, though this data was not exclusive to neonates. Turcotte (2019) (42) conducted another study using University of Louisville's NICU data for UPEs between November 2017 and December 2018. The data sample was small (n=22), with 18.2% of UPEs occurring in infants receiving continuous sedation, and 81.8% in infants receiving no/inadequate sedation. While studies showed continuous sedation could reduce UPE events due to less patient movement, it is important to note that there could be other side-effects, such as neurodevelopmental impairment (43), increased morbidity and even mortality (44-46). In addition, da Silva et al. (2013) (20) conducted a review of existing literatures to understand the impact of sedation use in NICU patients. Unfortunately, conclusions were inconsistent, and many studies had significant methodological flaws. There still remain gaps with respect to the sedation impact on UPEs for NICU patients.

2.3.5 Impacts of Physical Restraint

Chisako (2016) (47) conducted a literature review to discuss various UPE prevention strategies for NICU patients. They described only one study (the da Silva systematic review (20)) examining the relationship of physical restraints and UPE rates for neonates and infants. da Silva et al. (2013) (20) found inconsistent data on the relationship between physical restraints and UPEs for NICU patients (n=4 studies). The percentage of patients with physical restraints at the time of UPE ranged from 35% (24) to 87% (25). Two studies found that the use of limb restraints did not differ between the infants who had a UPE compared to those who did not. On the other hand, Little et al. (1990) (25) found in 58% of UPE cases, infants had two or less point of restraints. Also Brown et al. (1988) (23) reported that head restraints may have reduced UPEs for the infants who were more agitated. However, da Silva et al. (2013) (20) concluded that methodological flaws hampered the interpretation of the results and highlighted the gaps in existing literatures on physical restraints and UPE for the neonatal population.

2.3.6 Impacts of ETT Type

There were very few studies describing the effect of ETT type (e.g., nasal, oral), on UPE events for NICU patients. Spence et al. (1999) (48) performed a systematic review of the effects of oral and nasal intubation on the incidence of complications for newborn infants who were mechanically ventilated. The authors found only two randomized trials (22, 49) with few significant differences in the number of complications between oral and nasal intubation for mechanically ventilated neonates. In one of the studies conducted by McMillan et al. (1986) (22), the nasal route method resulted in higher rates of intubation failure (13.3%; 6 out of 45) compared with 0% (0 out of 46) for oral route intubation (RR 13.28, 95% CI 0.77, 229.08). The other study by Spitzer et al. (1982) (49) did not report intubation failure rate for nasal and oral methods, however atelectasis occurred for 34.9% (15 out of 43) nasally intubated infants compared to 11.6% (5 out of 43) orally intubated infants (RR 3.00, 95% CI 1.20, 7.53). On the other hand, McMillan et al. (1986) (22) observed the rate of post extubation right upper lobe atelectasis was not significantly different between oral and nasal methods (RR 1.28, 95% CI 0.65, 2.53). Neither of these studies found significant differences in UPE rates between the nasal and oral intubation. Spence et al. (1999) (48) suggested to interpret the results with caution when comparing the two methods, as the data samples were small.

2.3.7 Impacts of Repeated UPE

Pavlek et al. (2021) (50) conducted a cohort study on neonates who experienced a UPE in a 5-year period, to understand repeated UPE events, short-term complications, as well as long-term morbidities. The authors reviewed 588 events for a tertiary NICU Unit involving 300 patients. One hundred and thirty-three infants (44% of UPEs) experienced at least two UPEs, and 167 infants (56% of all UPEs) experienced one UPE. The group with greater than one UPE was found to have lower median GA at birth and PMA at the time of the UPE. This group was also found to have a greater number of ETT days, and experienced short-term adverse events compared to the group with only one UPE. A total 470 UPEs required re-intubation within 60 minutes, 166 received sedation, 196 required more than one attempt to re-intubate the infants, and 183 required deeper ETT positioning compared to previous ETT position. The impact of repeat UPEs was also observed by Thomas et al. (2017) (51) in a neonatal retrospective case-control study to analyze risk factors associated with severe subglottic stenosis (SASGS) requiring surgical intervention. Infants with SASGS were more likely to have a UPE event (p=0.007), an episode of traumatic intubation (p=0.003), oversized ETT (p=0.001) and more than 7 ETT days (p=0.0001). After conducting a multi-variate analysis, the author found infants with previous UPE experience had a higher risk (aOR =6.4 (1.65 to 24.77 at 95% CI) of SASGS.

2.3.8 Other Risk Factors

In addition to patient characteristics, other factors could also be associated with UPEs. The frequency of UPEs associated with poor tube fixation (loose tape) ranged from 8.5% (23) to 31% (12) of total of UPEs (median 31%, IQR 14.9 –37.5%). One study (29) estimated that MV duration was the only independent predictor of UPE; each day on MV increased UPE risk by 3% (relative risk 1.03, p=0.001). Three studies (24, 26, 31) addressed workload, particularly for nurses, and found no significant association with UPEs. For example, Veldman et al. (2006) (31) observed a higher patient-to-nurse ratio during UPE with a median of 3.85 (ranging 1.8 to 5 patients per nurse) compared to a median of 3 (1.6 to 6 patients per nurse), but this difference was not significant.

2.4 Summary and Conclusions

The literatures described in this review, provide an understanding of different strategies to reduce UPEs, and different risk factors associated with UPEs. Both topics vary widely in the literatures. Strategies that included multiple interventions (11, 12, 16), accurate data collection and documentation (8, 12), limited nursing workload and patient-to-nurse ratios (11), standardized procedures (13), and improved team communications (10, 52) resulted in improved rates of UPE. The studies (7, 9, 18, 19) where strategies did not significantly reduce UPE rates did not account for other risk factors such as patient characteristics and health provider education, which were potentially confounded by policy changes in the hospital. There were many different risk factors associated with UPEs. Factors might be related to patients' characteristics, circumstances of the events, as well as other factors. The influence of potential risk factors such as sex, GA, BW, patient movement, self-extubation, ETT manipulation, and sedation are variable, and others such as physical restraints and ETT types were not well described.

This literature review highlights gaps describing the impacts of longer term UPE reduction implementation strategies, the risks associated with UPEs, and clinical outcomes of infants who experience a UPE, especially those admitted to the NICU. Studies contributing to this knowledge base, may inform other neonatal institutions on how to develop a framework that could be used for future research and relevant clinical practices.

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Chapter 3. Manuscript

Characteristics of and Implementation Strategies used to Reduce Unplanned Extubations in the Neonatal Intensive Care Unit at The Hospital for Sick Children

3.1 Abstract

Background: Unplanned extubation (UPE) is the premature or unintended removal of an artificial airway (endotracheal tube, ETT). UPE events for neonates in the Neonatal Intensive Care Unit (NICU) can pose serious health risks for the neonates. This research describes the various UPE reduction strategies implemented over 10 years, at The Hospital for Sick Children (SickKids), and their impact on reducing UPEs. This research also describes contributing factors and patient characteristics of infants who had a UPE, and compares between biological sexes.

Methods: This study used a retrospective cohort study of all UPEs (excluding blocked ETTs) that took place between January 1, 2007 and December 31, 2019. Items collected included patient specific outcomes, UPE specific outcomes, and rate of UPE per 100 (mechanical) ventilation days (calculated). Detailed UPE data were recorded between July 2009 to December 2019 (prior to July 2009 only number of UPE, and ventilator days were collected). Descriptive analyses of UPE reduction strategies were based on NICU documents, and input from the RT lead in the NICU at the time. Comparisons of sex were planned a-priori. Comparisons between infants ≥32 and <32 weeks gestational age (GA) were completed because of a bimodal distribution. Other comparisons were completed for exploratory reasons. Comparative statistics included chi-square, (categorical variables), Welch's test (for continuous variables) or Wilcoxon rank sums tests (for skewed variables), with Bonferroni post-hoc pairwise comparisons on significant variables with greater than two items. Two multiple linear regressions were completed with duration of mechanical ventilation (MV), and NICU length of stay (LOS) as dependent variables. A p-value <0.05 was considered significant.

Results: The study sample included 302 cases (257 infants) of UPEs with 45 (12%) repeats in 31 infants. UPE/100 ventilator days decreased from 2.38 to 0.45 from 2003 to 2019 after six major implementation strategies (five Plan-Do-Study-Act cycles), and stayed below yearly target goals. Key strategies included long-term goals with standardized evaluation and documentation, incorporation into the NICU culture, institutional support, consistent education, and good communication. There were n=141

(55%) males, with average (SD) GA 30.8 (5.7) weeks. Infants with >1 UPE (compared to ≤ 1) had significantly lower weight (at UPE) and GA, had higher duration of MV and NICU LOS, less oral ETT but higher nasal ETT use, and had a lower proportion of sedation concerns. More males (n=129, 92%) compared to females (n=94, 82.5%) received the SickKids NICU taping protocol compared to other protocols, $p<0.05$. Infants ≥32 weeks GA had significantly higher weight, less UPEs, were younger when the UPE occurred, lower duration of MV and NICU LOS, more sedation concerns, greater use of restraints, less incidence of loose tapes, and less use of NICU taping protocol. Regression analyses found for every one day increase in age at UPE, the duration of MV increased by 0.65 days ($p<0.0001$, 95%CI 0.40 to 1.0 day), and NICU LOS increased by 0.922 days ($p<0.0001$, 0.7 to 1.2 days). If an infant had a repeat UPE, the duration of MV increased by 41.3 days ($p<0.0001$, 23.8 to 58.8 days), and NICU LOS increased by 32.7 days ($p<0.0001$, 15.2 to 50.2 days). For every one gram increase in weight, the NICU LOS decreased by 0.01 day or 20.2 minutes ($p=0.006$, 6 to 30 minutes).

Conclusions: Detailed and well planned UPE reduction strategies implemented over a 12-year period in the SickKids NICU significantly reduced the rate of UPEs. UPE characteristics and infant morbidity did not differ between biological sexes. For GA, the incidence of UPE occurred in a bimodal pattern (at 32 weeks). Infants with repeat UPE had longer duration of MV and NICU LOS, while those older at the UPE were associated with a reduction in these outcomes. Future research should explore implementation strategies in more detail using established frameworks. Studies should investigate factors associated with UPE, with multi-site data, registries, and/or prospective designs. This will help other healthcare facilities as well as researchers to develop their own implementation framework to reduce UPEs, and improve patient outcomes.

Keywords: unplanned extubation, UPE, neonate, mechanical ventilation, NICU, implementation strategies

3.2 Introduction

Mechanical ventilation (MV) is a life supporting treatment to help patients when they are unable to breathe by themselves. In most cases the process is used to support patients with respiratory, neurological, and cardiac failure (53-58). MV delivers positive pressure in order to take over or regulate an individual's breathing through an open airway such as an endotracheal tube (ETT) (59-62). Extubations are considered successful when weaning and removal of the ETT from MV are performed as per the medical team's plan.

Unplanned extubation (UPE) on the other hand, is the premature or unintended removal of an artificial airway (ETT, tracheostomy tube) by the patient or staff (14, 63). UPEs are often associated with infant agitation (including head turning), suctioning, loose tapes, ETT taping or re-taping, length of tube too short between the lip and the ETT adapter, and procedures (weighing, bathing) (23). In the neonatal intensive care unit (NICU), across different studies the UPE rate varied largely between 1% and 80.8% (median 18.2%), or from 0.14 to 5.3 UPEs/100 ventilator days (20). As neonates in NICU are admitted for specialized care such as prematurity, cardiorespiratory pathologies, infections, any UPE event could pose significant health risks for them.

The Hospital for Sick Children (SickKids) NICU in Toronto has undertaken actions suggested by the Society for Airway Management and the Patient Safety Movement Foundation actions(64), and implemented various strategies between 2007 to 2019. In 2008 the SickKids NICU created a "Reduce Unplanned Extubation" (RUE) Team, spearheaded by respiratory therapists (RT). It consisted of an interprofessional team that included RT, nursing, medicine (neonatology, anaesthesia), quality & safety, and the Acute Care Transport Services (ACTS). In addition, caregivers were included on issues relevant to them (e.g., transitions to infant holding), and the NICU Systems Analyst to verify and support documented UPEs in the hospital medical records. The RUE Team's purpose is to evaluate baseline data and develop quality improvement (QI) interventions to help reduce the rate of UPE in the NICU by 50% using the "Plan-Do-Study-Act" (PDSA) cycle (65). By 2019, the RUE Team completed five PDSA cycles that included multiple and standardized strategies, and still continues today.

This study focused on the following two objectives: 1) to describe the implementation strategies used to reduce UPE in the SickKids NICU, and their influence on UPE rates in the SickKids NICU, and 2) to describe contributing factors and patient characteristics of infants who had a UPE, and compare them between biological sex (male, female). Based on the literatures, we hypothesized that male infants would experience more UPEs, and worse outcomes compared to female infants. Describing the methods and strategies behind these successes could help other neonatal health care institutions standardize other treatments using a similar UPE reduction framework.

3.3 Methods

3.3.1 Study Design

This study used a retrospective cohort study of all UPEs in the SickKids NICU that took place between January 1, 2007 and December 31, 2019. The NICU at SickKids is the largest of its kind in Toronto, Canada. It is a level three, 42 bed fully outborn unit (36 beds at the time of this study), with about 850 admissions and 3600 ventilator days per annum. The sample size for this study was one of convenience; all available cases were included. This study was approved by the research ethics boards of SickKids (#1000066879), and Ontario Tech University (#16110).

3.3.2 Outcomes

All UPE reduction implementation strategies were documented in the SickKids electronic medical records (EMRs), safety reporting system, and within RUE Team documents (e.g., meeting minutes). All data on infants who had a UPE came primarily from hard copy “blue sheets” with additional information obtained from the hospital EMRs by the Systems Analyst in the NICU, and the lead RT at the time. Any UPE due to a blocked tube was excluded.

Patient specific outcomes included: sex, gestational age (GA), chronological age (at the UPE), weight at UPE, NICU length of stay (LOS), and duration of MV. UPE specific outcomes included: date of intubation, date of UPE, reason for intubation, use of high frequency jet ventilation (yes, no), type of ETT (oral, nasal), presence of excessive secretions (yes, no, and location), patient procedures at/or prior to UPE (self extubation, handling/holding/re-positioning, re-taping ETT, patient transfer, diagnostic imaging, tube insertion, routine assessment, suctioning, bathing, blood work, changing linen, changing incubator or bed), sedation concerns (yes [inadequate pain and/or agitation relief], no, if yes: name of sedation medication and date and time sedation last given), restraints used (yes, no), loose tapes (yes, no), other tubes present (nasogastric tube, repogle), original ETT taping protocol (NICU method, operating room tapes, referral hospital tapes, taped by transport team, modified taping method [if none was noted, NICU method was assumed]), date of last re-tape, date of last chest X-ray (CXR), last ETT position, was the patient re-intubated (yes, no), rate of UPE per 100 ventilator days (calculated).

3.3.3 Data Analysis

Detailed analyses were completed on UPE data between July 2009 to December 2019. This includes 11 April to April fiscal years, except 2009/2010 which included July to April only, and 2019/2020 April to December only. Prior to July 2009, there were no yearly target UPE rates, or details on each UPE (number of UPE, and ventilator days only). Chronological text summaries of all UPE reduction strategies implemented over this timeframe were provided.

If an infant experienced more than one UPE, only the first UPE recorded was included in the main quantitative comparative analyses. It allowed making comparisons between infants with more than UPE and one UPE. Descriptive statistics included rate of UPE (per 100 ventilator days) after each implementation strategy, and aggregating all data from the blue sheets and EMRs. All quantitative data (patient characteristics and descriptive variables) were presented using means and standard deviations (SD) and medians and interquartile ranges for continuous variables; and counts and proportions for categorical variables. Variables between males and females were compared using chi-square (for categorical variables), two-sample t-test (for continuous variables) or Wilcoxon rank sums tests (for skewed variables).

Comparisons between infants ≥32, and those <32weeks GA were completed because of the bimodal distribution pattern found in our study sample (19, 20, 28, 31). Other comparisons were completed for exploratory reasons (66), based on results from past literatures (procedures done prior to UPE(8, 19, 20, 26, 27, 38, 39), sedation concerns(20, 40-42), restraint use(47) (20, 23-25), loose tapes(23), ETT type(22, 48, 49)), and to determine if strategies specific to the SickKids NICU influenced different outcomes (taping protocol). Procedures done prior to UPE (yes, no) and taping protocol (NICU, other) were dichotomized for comparison. For 'between group' comparisons, the Welch's test was used to compare weight, GA; Wilcoxon-Mann Whitney test was used for skewed data -age at UPE, number of repeat UPE, duration of MV, and NICU LOS; and Chi-square test for proportions (with Bonferroni post-hoc pairwise comparisons). Two multiple linear regressions were completed with duration of MV and NICU LOS as dependent variables. Independent variables included in these two models were the continuous variables (weight, GA, age at UPE), and the categorical variables statistically significant in the bivariate comparisons. Using the rule of 10 participants per independent variable for multivariate regression modelling (F-test with significance level of 0.05, R-Squared of 0.10, and 90% power (67)), a maximum 25 independent variables could be included.

A p-value <0.05 was considered significant. IBM® SPSS® Software Platform was used to perform analyses.

3.4 Results

The study sample included a total of 302 cases of UPEs that occurred between April 1, 2009 and December 31, 2019. It was found that 45 (12%) of these were repeat UPEs in 31 infants.

3.4.1 Implementation Strategies

The number of UPE, ventilator days, and strategies implemented (2003 to 2019) are described in Table 1. The UPE per 100 ventilator days declined since 2003, and been below the target set for each fiscal year (Figure 2).

Table 1 UPEs and strategies over the fiscal years

Fiscal Years (Apr 1 - Mar 31)	UPEs*	Ventilator Days	UPE/ 100 Ventilator Days (target)	Strategies and Explanations
2003-2004	92	3866	2.38	
2004-2005	102	3789	2.69	
2005-2006	144	4161	3.46	
2006-2007	88	4589	1.92	
2007-2008	77	4226	1.82	ETT holder 6-month trial
2008-2009	91	3899	2.33 (50% ↓)	RUE QI Team (7 standards of care i.e., taping method, ETT care standards, contributing factors sheet, safety reporting)
Jul 2009-Apr 2010	57	4489	1.27 (<1.5)	Post UPE event huddles (with caregivers present), weekly discussions at safety rounds (contributing factors and prevention strategies).
2010-2011	43	4555	0.94 (<1.5)	Adjudication for blocked ETTs vs UPEs
2011-2012	42	4232	0.99 (<1.5)	
2012-2013	22	4554	0.48 (<1.5)	
2013-2014	35	3601	0.97 (<1.2)	Suture free ETT taping, creation of a neonatal weaning and extubation readiness protocol
2014-2015	32	3467	0.92 (<1.2)	Amendments to NICU taping protocol
2015-2016	32	3808	0.84 (<1.0)	
2016-2017	17	3737	0.45 (<1.0)	
2017-2018	23	4349	0.53 (<0.8)	
2018-2019	6	4233	0.14 (<0.8)	
Apr 2019-Dec 2019	13	2916	0.45 (<0.8)	

*Includes all UPEs, including repeats; target UPE/100 ventilator days were not introduced until 2009. ETT=endotracheal tube; NICU=neonatal intensive care unit; QI=quality improvement; RUE=reduce unplanned extubation; SBT=spontaneous breathing trial; UPE=unplanned extubation.

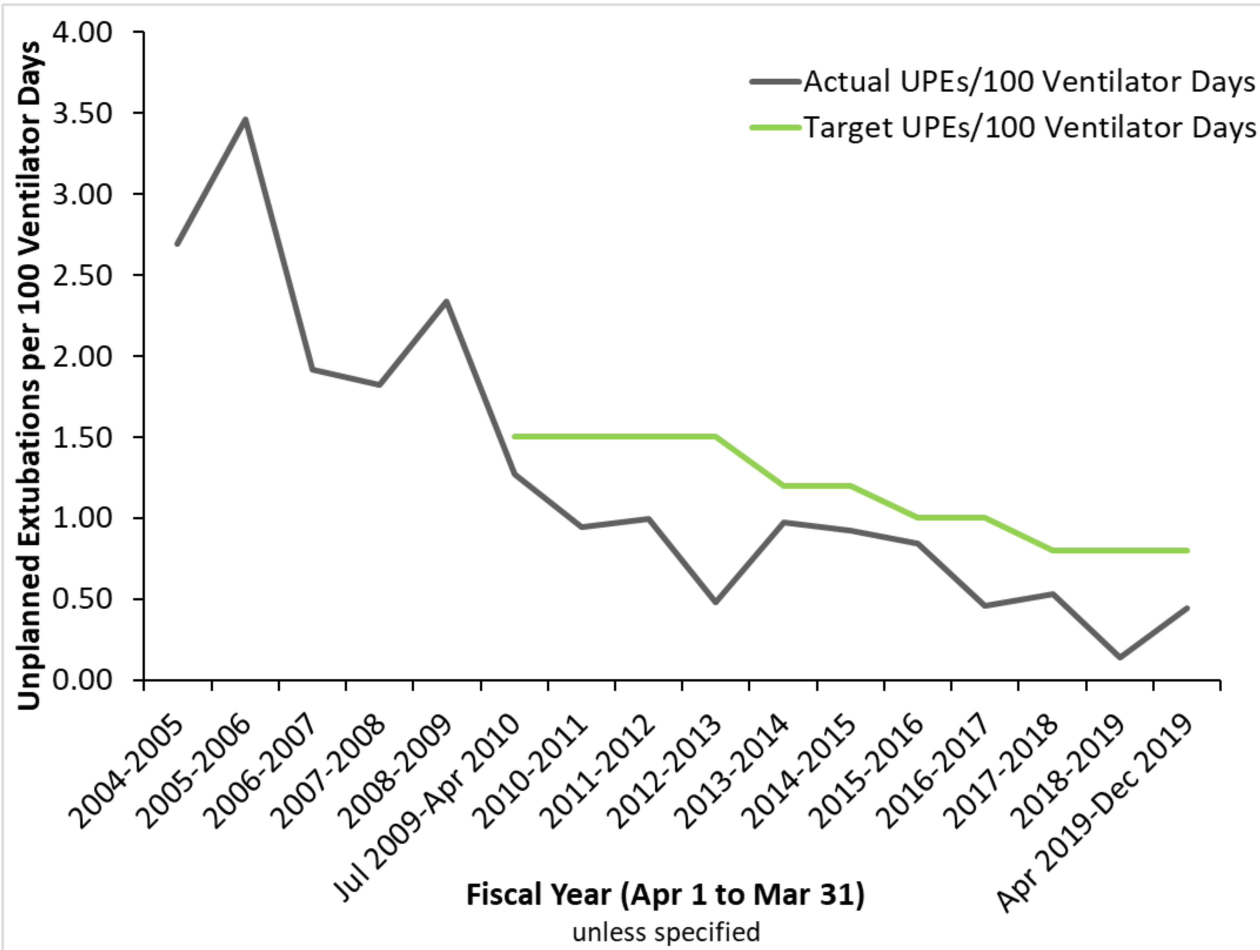

Figure 2 The number of actual unplanned extubations (UPEs) per 100 ventilator days (grey line) for each fiscal year (unless specified). Target UPE/100 ventilator days (green line) were not introduced until 2009.

The first UPE reduction strategy that was rolled out in the SickKids NICU occurred in 2007/2008 with a six-month ETT holder trial. The number of UPEs per 100 ventilator days did not substantially change, and even increased (1.92 at the end of 2007, 1.82 end of 2008, 2.33 end of 2009, Table 1). After this time (2008-2009) the NICU RUE QI Team was established (still in existence). The RUE Team consists of interprofessional members whose mandates are to 1) collect data from medical charts and safety reports to track NICU progress on reducing UPEs; 2) establish a common target threshold for UPEs; 3) establish care standards for infants with ETTs; 4) develop further interventions and tools to address trends and/or common elements associated with UPEs; 5) develop and maintain a mechanism to ensure all UPEs are documented consistently; and 6) provide timely knowledge dissemination, and educational plans for health providers and caregivers. The group meets monthly, with ad hoc meetings as necessary. An initial environmental scan revealed approximately 2.0 to 3.0 UPEs per 100 ventilator days occurred in the NICU. This was likely underestimated as UPEs were being tracked as a hospital safety event about 60% of the time. UPEs were not being reported for patients deemed ready for extubation, or “doing fine” after the event (indicating a general lack of appreciation for the risks associated with UPEs). In addition, taping methods varied, were modified or adjusted about 30% of the time.

To help meet the RUE Team’s objectives, two phases were planned and launched. Phase 1 included: 1) evaluating NICU UPE numbers, and how they compared with the literature; 2) developing standards of care for infants with ETTs; 3) developing an educational roll out plan for the new standards (for the whole interdisciplinary team); 4) developing tools (e.g., checklists) to aid in standardized practices; and 5) developing a mechanism to ensure all UPEs were captured within the safety reporting system. Phase 2 included a six-month evaluation of UPEs after implementing seven evidence-based standards of care: 1) ETTs consistently secured using the NICU taping method (including patients from referral centres and the operating room). These inter professionally developed taping protocols included indications, precautions, materials to use, detailed steps, photographs, and educational materials. Any taping modifications required documentation in the medical chart, and review by member of the RUE Team; 2) decreased pressure points on patients’ nare or mouth by minimizing tension on the ETTs and ventilator tubing (monitored hourly); 3) establishing two-person procedures where one person maintained position of the ETT and provided comfort to the patient, while the other performed the procedure. Procedures included X-rays, line insertions, weighing, handling (difficult airways), suctioning on high frequency jet ventilation or high frequency oscillatory ventilation; 4) ETT tapes and need for re-taping assessed and documented in the medical chart by the RT a minimum twice per shift. RTs also assessed (with anaesthesia) all post-surgical patients with ETTs (all of these patients were re-taped with the NICU protocol within one hour of admission to the NICU); 5) loose tapes (>0.5cm slack and tapes lifted from upper lip) were immediately communicated to the RT; 6) intubated patients nasally/orally suctioned as needed in order to prevent secretions and loose tapes; and 7) patients extubated when clinically ready and in collaboration with the medical team regardless of time of day (with consideration of shift changes).

A benchmark was set to reduce UPEs by 50%, and increase reporting to 100%. Roll out of these seven standards were accompanied with a detailed communication and education plan, posting of laminated acronym/reminders on all ventilators (E-T-T-C-A-R-E, Figure 3), and dedicated hard copy "blue sheet" (Figure 4), and safety report forms and processes. These standards of care and processes made a large difference, with UPEs going from 2.33 to 1.27 per 100 ventilator days (exceeding the 50% benchmark), and 100% of UPEs formally reported as safety events.

Continuing with the initial success of the RUE Team's initiatives, yearly benchmarks were set and strategies added and/or amended (based on common trends). UPE processes, encounters and discussions were being incorporated in the NICU culture. This included using UPE experiences as teachable moments. In 2009/2010, "huddles" (with caregivers present) were introduced after every UPE occurrence. Any UPE that occurred was discussed (contributing factors, prevention strategies) at weekly NICU safety rounds (formerly called "morbidity and mortality" or M&M rounds), quality management team forums, and monthly safety group meetings. Some trends/themes identified during these sessions included: the two-person procedure for chest X-rays not being followed, UPEs occurring during caregiver holding (e.g., skin-to-skin "kangaroo care"), difficult airway alert signs missing, and restraints for high-risk patients (e.g., tracheoesophageal fistula) not being utilized. These trends resulted in process changes including: RT involvement in all chest X-rays; establishing processes and standard responsibilities for the nurse(s), RT, and caregiver for high-risk transfers/repositioning/kangaroo care; and putting infants that experienced more than one UPE on "high alert" along with creating signage by the bedside (labelled "AIRWAY"). Finally, UPEs were routinely included in mock codes, education days, new hire orientation, and simulation scenarios. Detailed educational training on UPE reduction strategies continued until it became a routine process in the NICU culture (about three years).

Between 2011 and 2013 all strategies continued to be put in practice. In 2010/2011 blocked ETTs were not deemed as UPE events (and quality metrics amended as a result), as it did not meet the definition of an unintended removal. At the end of 2011, a detailed analysis found that approximately 50% of patients that had a UPE did not require re-intubation. As a result, a new weaning and extubation readiness protocol (68) was developed and launched. It was also discovered that patients on longer durations of MV required ETT replacements because suturing tubes created holes and leaks. This suturing securement method was unique to SickKids, based on one study(69) showing a reduction in UPEs compared to non-suturing methods (statistical significance unknown(70), assessment period five months, nursing perspective). This method involved attaching a silk suture to a small piece of tape on the infant's upper lip, then suturing through the ETT. This was performed on both the left and right sides, and any re-taping required re-suturing. In addition to creating leaks, there were increasing needle stick injuries while suturing the ETT in place. As a result of this, a suture free campaign was launched (2013/2014), and the NICU taping protocol revised accordingly. Some people in the NICU found this change particularly difficult because the technique had been entrenched for over 30 years.

Further changes to the NICU taping technique continued into 2014 and 2015 including: avoiding use of chemicals to remove tapes and adhesive residue (due to the toxicity and oily properties), using cheek protection barrier dressings (to prevent contact of adhesive directly on skin), no reinforcement of pre existing tapes, wrapping tapes around the tube three times with 50% overlap onto previous wrap (candy cane technique), folding the end of the tape to create a tab to facilitate easy removal of tapes during retaping, folding a second tape at the site of the opposite nare to avoid occlusion, using one type of tape only, standardized taping kits (made by RTs), and considering different methods based on patients' facial skin integrity. Table 2 summarizes the SickKids UPE reduction strategies and their successes, between 2007 and 2019.

Table 2: Summary of SickKids UPE Reduction Strategies

Strategy	**Details of Strategy**
2007: ETT holder trial	The first UPE reduction strategy that was rolled out in the SickKids NICU occurred in 2007 with a six-month ETT holder trial. The number of UPEs per 100 ventilator days did not substantially change, and even increased (1.92 at the end of 2007, 1.82 end of 2008, 2.33 end of 2009)
2008: NICU Reduce Unplanned Extubation (RUE) QI Team establishment	It consisted of an interprofessional team that included RT, nursing, medicine (neonatology, anaesthesia), quality & safety, and the Acute Care Transport Services (ACTS). The mandates of the RUE team were to 1) collect data; 2) establish a common target; 3) establish care standards; 4) develop tools to address trends and causes; 5) document events consistently; and 6) knowledge sharing. The RUE Team developed 7 standards of care to reduce the rate of UPE in the NICU by 50% using the PDSA cycle. These standards of care and processes reduced UPEs going from 2.33 to 1.27 per 100 ventilator days (exceeding the 50% benchmark)
2009: Post UPE event huddles	"Huddles" (with caregivers present) were introduced after every UPE occurrence. Any UPE that occurred was discussed

	(contributing factors, prevention strategies) at weekly and monthly meetings. Some trends/themes were identified during these sessions and resulted in process changes including: RT involvement in all chest X-rays; establishing processes and standard responsibilities for the nurse(s), RT, and caregiver for high-risk transfers/repositioning/kangaroo care; and putting infants that experienced more than one UPE on “high alert” along with creating signage by the bedside. As a result, UPEs went from 1.27 to 0.94 per 100 ventilator days
2010: Adjudication for blocked ETTs vs UPEs	In 2010/2011 blocked ETTs were not deemed as UPE events as it did not meet the definition of an unintended removal. At the end of 2011, a detailed analysis found that approximately 50% of patients that had a UPE did not require re-intubation. As a result, a new weaning and extubation readiness protocol was developed and launched. This strategy kept the UPE rates below the target of 1.5 UPEs per 100 ventilator days
2013: Suture free ETT taping	It was discovered that patients on longer durations of MV required ETT replacements because suturing tubes created holes and leaks. This suturing securement method was unique to SickKids. This method involved attaching a silk suture to a small piece of tape

	on the infant's upper lip, then suturing through the ETT. In 2013, a suture free campaign was launched, and the NICU taping protocols were revised accordingly. UPE rates reduced and were kept below the target of 1.2 per 100 ventilator days
2014: Amendments to NICU taping protocol	Many changes were made to the NICU taping technique including avoiding use of chemicals to remove tapes and adhesive residue (due to the toxicity and oily properties), using cheek protection barrier dressings (to prevent contact of adhesive directly on skin), no reinforcement of pre existing tapes, wrapping tapes around the tube three times with 50% overlap onto previous wrap (candy cane technique), folding the end of the tape to create a tab to facilitate easy removal of tapes during retaping, folding a second tape at the site of the opposite nare to avoid occlusion, using one type of tape only, standardized taping kits (made by RTs), and considering different methods based on patients facial skin integrity. UPEs were kept below the target of 1.2 per 100 ventilator days

Throughout the five PDSA cycles, a number of key success factors were identified. These included setting achievable goals, ensuring strategies were evaluated, amending or developing strategies in response to trends, maintaining consistency with the strategies (and documentation) continuously over the long-term (not relying on short-term outcomes or fixed timeframes), incorporating it as part of the NICU culture, institutional support and validation, and promoting good communication by being honest and “real”, sharing the commitment, and sharing successes. In addition, educational blitzes were (and are) routinely organized to refresh staff on the UPE strategies, and re-iterate the importance of safety reporting; stressing it is not a punitive or “shame and blame” tool but one that highlights system issues, organizes solutions to minimize risk to the patient, and provides a safe environment.

E•T•T•C•A•R•E

Ensure tube is secured (NICU taping method)

Tubing tension eliminated

Two person procedures

CIMS documentation required

Assess appearance often

Retape as required

Extubate when clinically ready

	E•T•T•C•A•R•E STANDARDS	RESPONSIBILITY
1	Endotracheal tubes (ETTs) will be consistently secured using the current NICU taping method by the RT/ACTS and the RN will assist. ETT's of patients from referral centers and the OR will be retaped within 2 hrs of arrival to Unit. Modifications, based on patient needs shall be documented on CIMS/reviewed on the ACTS call back with the transport co-coordinator and MD. The practice of reinforcing ETT tapes is not acceptable.	RT/ACTS
2	Tension on the ETTs and ventilator tubings will be minimized using appropriate tubing holders as required: position ETT's to eliminate pressure points on the nare/mouth and monitor hourly.	RN/RT/ACTS
3	Two Person procedures for intubated patients shall include: X-rays, line insertions, weighing, handling of infants with difficult airways, suctioning infants on HFJV or HFOV. One person maintains the ETT and provides comfort to the patient and the other person performs the necessary positioning/procedure.	RN/RT/ACTS
4	ETT tapes and the need for retaping shall be assessed and documented in CIMS by the RT a minimum of 2X per shift. In the post op patient, the RT must obtain pertinent airway information from anaesthesia/ENT (i.e. TEF repairs, difficult airways etc.)	RT
5	Loose ETT tapes (> 0.5 cm play and/or ETT tapes have lifted from the upper lip) shall be immediately communicated to the RT by the RN. The RT will assess the need for re-taping and document accordingly in CIMS.	RN & RT
6	Intubated patients require nasal/oral suctioning as needed to prevent secretions from loosening the tapes.	RN/RT
7	Patients will be extubated when clinically ready and in collaboration with the medical team regardless of the time of day. Consideration should be given around shift change.	RT/MD/ CNSNP/RN

Figure 3 E-T-T-C-A-R-E: laminated UPE standards of care acronym/reminders

(posted on all ventilators)

CONTRIBUTING FACTORS TO UNPLANNED EXTUBATIONS		
SAFETY REPORT MUST BE FILLED OUT:		RT NAME**:**
PT. NAME:	**ID/MRN:**	**DATE:**
HFV? ____Yes ____NO		
DATE & REASON FOR INTUBATION		
ORAL		**COMMENTS:Post huddle with RN**
NASAL		
EXCESSIVE SECRETIONS		
DURING PT PROCEDURE		
	IV insertion	
	X-ray	
	LP	
	Blood work	
	Bathing	
	Changing Linen/BED	
	Routine Cares: reposition/sxn	
	Retaping ETT	
SEDATION RELATED?		
	Medication infusion/bolus	
	Last given	
	Restaints	
LOOSE TAPES?		
OTHER TUBES PRESENT?		
	NG tube	
	Repogle	
NICU TAPING PROTOCOL?		
	OR ETT Tapes	
	Referral Hospital Tapes	
	Modified Taping Method	
	Date of last retape	
BLOCKED ETT? NOT=UPE!		
	Mucus/Blood plug	
	During BLES admin	
LAST CXR & ETT POSITION		
PATIENT REINTUBATED?		

Figure 4 Blue sheets requiring completion for each UPE event.
This document was revised and updated over several PDSA cycles.

3.4.2 Characteristics of UPEs

For infants with two more UPEs, only the first UPE recorded was included in subsequent comparative analyses (n=257). These infants (compared to those who had one UPE) had significantly lower weight, lower GA, had higher duration of MV and NICU LOS, less oral ETT but higher nasal ETT use, and had a lower proportion of sedation concerns (Table 3). There were no significant differences in biological sex, restraint use, proportion with loose tapes, proportion who had procedures done prior/at UPE occurrence, or in the taping protocol (Appendix Table A1).

Table 3 Comparison of infants with and without repeat UPE (significant differences only)

Variable	**Repeat UPEs**		
	Yes, n=31	**No, n=226**	**p-value**
Number of UPEs, Mean (SD)	2.45 (0.77)	1.00 (0.00)	<0.0001
Weight (grams), Mean (SD)	1,525.7 (984.4)	2,199.6 (1185.4)	0.003
GA (weeks), Mean (SD)	28.0 (4.5)	31.2 (5.8)	0.003
GA > 32 weeks, N(%)	7 (22)	105 (46)	0.01
Duration of MV (days), Median (IQR)	69.0 (26.0-125.0)	13.0 (4.0-52.0)	<0.0001
LOS NICU, Median (IQR)	90.2 (38.6-137.3)	31.6 (11.9-75.2)	<0.0001
Sedation concerns, N(%)	3 (10)	60 (27)	0.04
Type of ETT, oral / nasal, N(%)	10 (32) / 21 (68)	120 (56) / 95 (44)	0.01

ETT=endotracheal tube; GA=gestational age; LOS=length of stay; NICU=neonatal intensive care unit; IQR=interquartile range; SD=standard deviation; UPE=unplanned extubation

Table 4 and, Figures 5 describes patient's characteristics as well as other UPE related details. There was n=141 (55%) males, the average (SD) gestation age 30.8 (5.7) weeks, weight at UPE 2,116.7 (1,181.8) g, and median (IQR) age at UPE 16.0 (5.0 - 38.0) days. There was a bimodal pattern for gestational age (Figure 6) showing a split at approximately 32 weeks. The median (IQR) length of NICU stay was 39.1 (13.2 - 80.0) days and the duration of MV 16.0 (5.0 - 57.0) days, suggesting about half of the NICU stay period for infants who had UPEs, was spent on MV. Sedation concerns was present for n=63 (25%) cases, loose tape for n=36 (14%) cases, and presence of excessive secretion for n=42 (16%) of cases. The most common procedures prior to UPE included n=61 (24%) self extubations, followed by n=44 (17%) infant handling or re-positioning.

The SickKids NICU taping protocol was used in n=225 (88%) of the infants who had a UPE. Both nasal and oral ETT methods were used fairly equally.

The date of the last chest X-ray was reported only in 11 instances, an average (range) 2.2 (0 to 7) days prior to the UPE. The date of the last re-tape was reported in 109 instances, an average 2.3 (0 to 10) days prior to the UPE. The last ETT position was reported in five instances, with n=2 reporting "good position", n=1 "T1", and n=1 stating intubation was carried out at the referral hospital. Use of high frequency jet ventilation was reported only in 5 instances. Types of sedation included Opioids (n=59), Benzodiazepines (n=11), and Chloral Hydrate (n=2). These were provided continuously (n=34), were being weaned (n=10), provided on the morning shift (n=3), or the evening shift (n-5).

Table 4 UPE characteristics: Whole cohort

Variable[a]	**All (n=257)**
Weight (grams) Mean (SD), Median (IQR)	2,116.7 (1,181.8), 1,969.0 (1,044.0 - 3,011.0)
Gestational age (weeks) Mean (SD), Median (IQR)	30.8 (5.7), 29.0 (26.0 -36.0)
Age at UPE (days) Mean (SD), Median (IQR)	26.3 (30.2), 16.0 (5.0 -38.0)
Duration of mechanical ventilation (days) Mean (SD), Median (IQR)	39.3 (52.6), 16.0 (5.0 -57.0)
Length of stay in NICU Mean (SD), Median (IQR)	55.6 (54.1), 39.1 (13.2 -80.0)
Number of UPEs Mean (SD), Median (IQR)	1.2 (0.5), 1.0 (1.0 -1.0)
Sex, N (%), n=2 missing	
• Male	• 141 (54.9)
• Female	• 114 (44.4)
Repeat UPE, N(%)	31 (12.1)
Sedation concerns, N(%)	63 (24.5)
Infants GA 32 weeks and older, N(%), n=3 missing	112 (43.6)
Patient restrained, N(%)	57 (22.2)
Loose tape, N(%)	36 (14.0)
Presence of excess secretions, N(%)	42 (16.3)
Procedures prior to/at UPE occurrence	
• Self extubation	• 61 (23.7)
• Handling, holding, re-positioning	• 44 (17.1)

• Re-taping ETT	• 17 (6.6)
• Patient transfer	• 18 (7)
• Diagnostic imaging	• 9 (3.5)
• Tube insertion	• 10 (3.9)
• Routine assessment	• 9 (3.5)
• Suctioning	• 9 (3.5)
• Bathing	• 6 (2.3)
• Blood work	• 3 (1.2)
• Changing linen	• 3 (1.2)
• Changing incubator or bed	• 3 (1.2)
Type of ETT, N(%)	
• Oral	• 130 (50.6)
• Nasal	• 116 (45.1)
Original ETT taping protocol	
• NICU taping protocol	• 225 (87.5)
• Operating room	• 13 (5.1)
• Referral hospital	• 2 (0.8)
• Transport Team	• 9 (3.5)
• No suture	• 3 (1.2)
• Over nose	• 2 (0.8)
• Sutured	• 2 (0.8)
• Other[b]	• 1 (0.4)
Reason for intubation, N (%)	
• Unstable airway/Respiratory Insufficiency	• 53 (20.6)
• Respiratory support in neonatal sepsis/Necrotizing enterocolitis	• 21 (8.2)
• Post-operative	• 19 (7.4)
• Congenital or structural airway abnormalities	• 8 (3.1)
• Severe meconium aspiration syndrome	• 3 (1.2)
• Extreme prematurity	• 3 (1.2)
• Seizure	• 2 (0.8)
• PPHN	• 2 (0.8)
• Other[c]	• 11 (4.3)
Other tubes present?	
• NG tube	• 145 (56.4)
• Repogle	• 2 (0.8)
• OG tube	• 8 (3.1)
• G tube	• 1 (0.4)

[a]Any variables that do not equal the total sample size under each column were either not reported or missing. [b]other: patient situation specific e.g., skin condition. [c]other: intubated at referral hospital, unknown.
ETT=endotracheal Tube; GA=gestational age; G tube=gastronomy tube; IQR=interquartile range; NG tube=nasogastric Tube; NICU=Neonatal Intensive Care Unit; OG tube=orogastric tube; PPHN=persistent pulmonary hypertension of the newborn; SD=standard deviation; UPE=unplanned extubation.

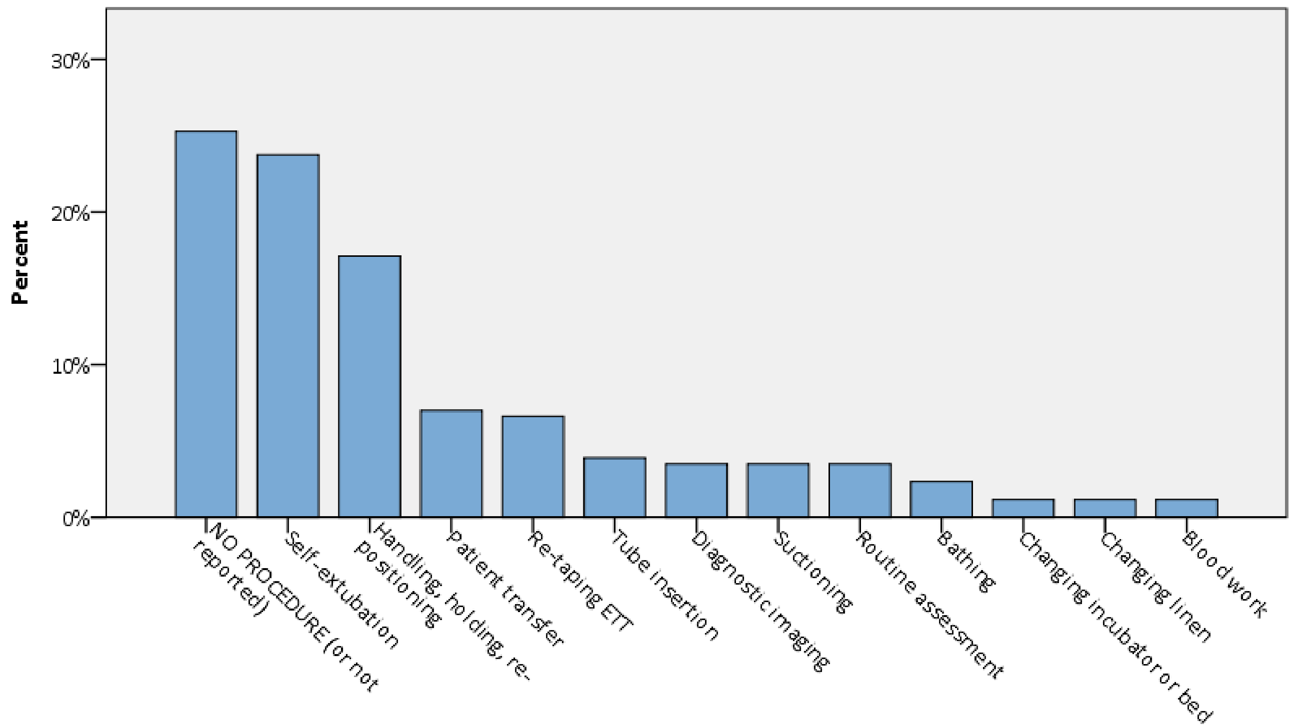

Figure 5 Distribution of different procedures prior to or at the time of UPE occurrence

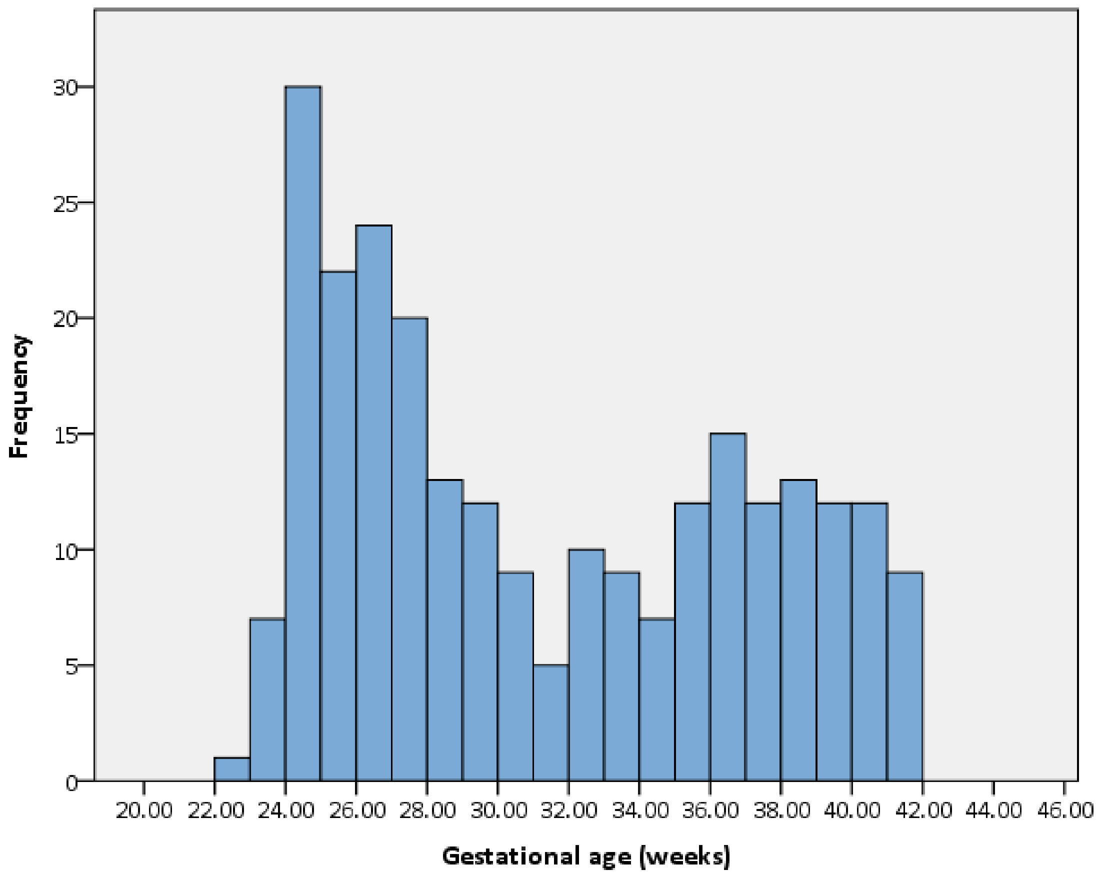

Figure 6 Frequency distribution of gestation age for the infants that had a UPE

3.4.3 Impact of Sex on UPE

Table 5 compares patient characteristics and other UPE related variables between males and females. The only significant result was the original taping protocol, with more males (n=129, 91.5%) compared to females (n=94, 82.5%) receiving the NICU taping protocol compared to other techniques, p=0.03.

Table 5 UPE characteristics: Sex

Variable	Female (n=114)	Male (n=141)	p-value
Weight (grams) Mean (SD), Median (IQR)	2,047.4 (1,325.5), 1,626.7 (968.0-2,968.8)	2,173.0 (1,052.3), 2,160.3 (1,143.4-3,026.8)	0.403
Gestational age (weeks) Mean (SD), Median (IQR)	30.6 (6.0), 28.0 (25.0-36.0)	31.0 (5.5), 30.0 (26.0-36.0)	0.603
Age at UPE (days) Mean (SD), Median (IQR)	25.8 (33.1), 16.0 (5.0-38.0)	26.6 (27.8), 16 (7.0-40.0)	0.543

Duration of mechanical ventilation (days) Mean (SD), Median (IQR)	40.7 (49.3), 20.0 (5.0-56.0)	38.1 (55.2), 15.0 (5.0-57.0)	0.806
Length of stay in NICU Mean (SD), Median (IQR)	55.6 (47.5), 46.6 (15.5-83.0)	55.8 (59.1), 31.9 (13.1-80.1)	0.444
Infants GA 32 weeks and older	48 (42.5)	64 (45.4)	0.642
Repeat UPE, N(%)	12 (10.5)	19 (13.5)	0.474
Sedation concerns, N(%)	30 (26.3)	33 (23.4)	0.592
Patient restrained, N(%)	26 (22.8)	31 (22.0)	0.876
Loose tape, N(%)	18 (15.8)	18 (12.78)	0.491
Presence of excess secretions, N(%)	19 (16.7)	22 (15.6)	0.818
Procedures prior to/ at UPE occurrence, N(%)			0.986
• Yes	• 29 (25.4)	• 36 (25.5)	
• No	• 85 (74.6)	• 105 (74.5)	
Type of ETT, N(%)			0.424
• Oral	• 54 (50.0)	• 75 (55.1)	
• Nasal	• 54 (50.0)	• 61 (44.9)	
Original ETT taping protocol			**0.030**
• NICU taping protocol	• 94 (82.5)	• 129 (91.5)	
• Other taping technique	• 20 (17.5)	• 12 (8.5)	

ETT=endotracheal tube; GA=gestational age; IQR=interquartile range; NG tube=nasogastric tube; NICU=Neonatal Intensive Care Unit; SD=standard deviation; UPE=unplanned extubation.

3.4.4 Impact of GA on UPE

Table 6 compares patient characteristics and other UPE related variables between infants ≥32, and those <32weeks GA. Infants ≥32 weeks GA had significantly higher weight, less (repeat) UPEs, were older when the UPE occurred, lower duration of MV and NICU LOS, more sedation concerns, greater use of restraints, less incidence of loose tapes, and less had the NICU taping protocol.

Table 6 UPE Characteristics: GA

Variable	**GA <32 weeks (n=142)**	**GA ≥32 weeks (n=112)**	**p-value**
Weight (grams) Mean (SD), Median (IQR)	1,446.1 (873.3), 1,161.9 (834.2-1,810.0)	2,968.4 (952.9), 3,017.0 (2,308.3-3,634.0)	**<0.0001**

Age at UPE (days) Mean (SD), Median (IQR)	33.1 (27.5), 23.0 (12.0- 49.0)	36.7 (2.8), 6.0 (3.0-19.0)	**<0.0001**
Duration of mechanical ventilation (days) Mean (SD), Median (IQR)	53.3 (52.9), 38.0 (16.0- 77.0)	21.6 (46.7), 6.0 (3.0-13.0)	**<0.0001**
Length of stay in NICU Mean (SD), Median (IQR)	71.9 (54.3), 60.6 (30.0- 100.0)	35.2 (46.8), 16.4 (9.6- 40.6)	**<0.0001**
Sex, N(%)			0.642
• Male	• 77 (54.2)	• 64 (57.1)	
• Female	• 65 (45.8)	• 48 (42.9)	
Repeat UPE, N(%)	24 (16.9)	7 (6.2)	**0.010**
Sedation concerns, N(%)	23 (16.2)	39 (34.8)	**0.001**
Patient restrained, N(%)	23 (16.2)	34 (30.4)	**0.007**
Was there loose tape, N(%)	27 (19.0)	9 (8.0)	**0.013**
Presence of excess secretions, N(%)	18 (12.7)	22 (19.6)	0.130
Procedures prior to/ at UPE occurrence, N(%)			0.101
• Yes	• 42 (29.6)	• 23 (20.5)	
• No	• 100 (70.4)	• 89 (79.5)	
Type of ETT, N(%)			0.089
• Oral	• 64 (47.8)	• 64 (58.7)	
• Nasal	• 70 (52.2)	• 45 (41.3)	
Original ETT taping protocol, N(%)			**0.003**
• NICU taping protocol	• 132 (93.0)	• 90 (80.4)	
• Other taping technique	• 10 (7.0)	• 22 (19.6)	

ETT=endotracheal tube; GA=gestational age; IQR=interquartile range; NICU=Neonatal Intensive Care Unit; SD=standard deviation; UPE=unplanned extubation.

3.4.5 Exploratory Analyses

Results of pairwise comparisons of UPE risk factors are found in Table 7 (statistically significant results only), and Appendices Tables A2 to A9 (all results).

Infants that <u>had procedures prior to, or at the UPE </u>(in comparison to those that did not) had significantly lower weight, longer NICU LOS, and lower oral but higher nasal ETT use. The proportion of infants with sedation concerns had significantly different procedures prior to, or at the UPE (p=0.05). Infants with no reported sedation concerns (compared to those with, appendix Table A8), self extubated less (n=38/194, 20% versus n=23/63, 37%), and had fewer routine assessments (n=5/194, 8% versus n=4/63, 2%), both p<0.05. The proportion of infants with loose tapes also had significantly different procedures prior to the UPE occurring (p=0.01). More infants with loose tapes had their ETT re-taped (n=10/36, 28%) compared to those that did not have loose tape (n=7/221, 3%), p<0.05. The proportion of infants with nasal ETTs also had significantly different procedures prior to the UPE occurring (p=0.03). More infants with nasal ETTs (29/116, 34%) compared to oral ETT (20/130, 15%) had no procedures reported, p<0.05.

Infants that had sedation concerns (in comparison to those that did not), had higher weight, higher GA, less (repeat) UPE, lower duration of MV and NICU LOS, more restraint use, less loose tapes, and a higher proportion receiving the SK NICU taping protocol. Infants that were restrained (in comparison to those that were not) had higher weight, higher GA, a higher proportion of sedation concerns, and higher proportion receiving the SK NICU taping protocol. Infants that had loose tapes (in comparison to those that did not) had lower GA, were older at UPE, longer duration of MV, had a lower proportion of sedation concerns, and had a lower proportion receiving the SK NICU taping protocol. Infants that had an oral ETT (in comparison to nasal ETT) had lower number of (repeat) UPEs, were younger at the UPE, lower NICU LOS, had less procedures prior to or at the UPE, and less received the SK NICU taping protocol. Infants that received the SK NICU taping protocol (in comparison to those that received other taping techniques) were older at the UPE, had shorter duration of MV and NICU LOS, had a higher proportion of sedation concerns, had lower proportion with loose tapes, and had a higher proportion of males but lower proportion of females. Infants with reported excessive secretion (in comparison to those that did not) had higher weight.

Table 7 Exploratory analysis of UPE characteristics (significant results only)

Variable	Procedure(s) prior/ at UPE		Sedation Concerns		Restrained		Loose Tapes		ETT Type		Taping Protocol		Excessive secretions	
	Yes n=65	**No n=192**	**Yes n=63**	**No n=194**	**Yes n=57**	**No n=200**	**Yes n=36**	**No n=221**	**Oral n=130**	**Nasal n=116**	**SK NICU n=225**	**Other n=32**	**Yes n=42**	**No n=215**
Weight (grams), Mean (SD)	1,857.7 (1,036.3)	2,206.7 (1218.1)	2,520.8 (1,095.1)	1,987.6 (1,182.1)	2,595.2 (1,117.6)	1,979.9 (1,166.6)							2,527.7 (1,104.2)	2,041.4 (1,182.5)
	0.04		0.002		0.001								0.018	
Age at UPE (days), Median (IQR)							19.0 (11.5-58.5)	15.0 (5.0-36.0)	11.0 (5.0-29.0)	9.0 (7.0-49.0)	18.0 (8.0-45.0)	12.0 (4.0-36.0)		
							0.05		0.002		0.006			
GA, Mean (SD)			33.1 (5.8)	30.1 (5.5)	32.3 (5.9)	30.4 (5.6)	28.9 (4.7)	31.1 (5.8)						
			<0.0001		0.02		0.03							
GA > 32 weeks, N(%)			39 (63)	76 (38)	34 (60)	78 (40)	9 (25)	103 (47)						
			0.001		0.007		0.01							
Duration of MV (days), Median (IQR)			11.0 (3.0-28.0)	23.0 (5.0-68.0)			39.0 (9.5-76.0)	15.0 (5.0-53.0)			11.5 (4.0-52.0)	23.5 (7.0-57.0)		
			0.01				0.04				0.008			
LOS NICU, Median (IQR)	57.8 (18.5-100.0)	35.5 (12.8-73.2)	21.3 (10.8-50.4)	47.4 (15.5-86.8)					24.40 (9.9-70.7)	48.8 (18.3-90.2)	24.4 (9.9-70.7)	48.8 (18.3-90.2)		
	0.03		0.007						0.003		0.03			
Sex, male/female, N(%)											83(63)/ 48(37)	58(47)/ 66(53)		
											0.008			
# of UPEs, Mean (SD)			1.08 (0.41)	1.21 (0.57)					1.11 (0.44)	1.27 (0.65)				
			0.04						0.01					
Repeat UPE, N(%)			3 (5)	28 (14)					10 (8)	21 (18)				
			0.04						0.03					
Sedation concerns, N(%)					24 (42)	39 (20)	2 (6)	61 (28)			40 (30)	23 (18)		
					0.0001		0.004				0.05			

Patient restrained, N(%)			24 (38)	33 (17)							55 (97)	2 (4)		
			<0.0001								0.020			
Loose tape, N(%)			2 (3)	34 (18)										
			0.004											
Procedures prior at UPE occurrence, N(%)									20 (15)	39 (34)				
									0.001					
Type of ETT, oral/nasal, N(%)	20 (34)/ 39(66)	110(59)/ 77(41)									109(51)/ 107(50)	21(70)/ 9(30)		
	0.001										0.045			
NICU ETT taping protocol, N(%)					55 (97)	170 (85)			109 (83.8)	107 (92.2)				
					0.02				0.045					

ETT=endotracheal tube; GA=gestational age; IQR=interquartile range; LOS=length of stay; MV=mechanical ventilation; NICU=Neonatal Intensive Care Unit; SD=standard deviation; UPE=unplanned extubation.

The multiple linear regression to predict duration of MV based on weight, GA, age at UPE, if infant had a repeat UPE, sedation concerns, loose tape, and ETT taping protocol is found in Table 8. These variables statistically significantly predicted duration of MV F(7, 243) = 14.282, $p < .0001$, $R^2 = 0.291$. Specifically, for every one day increase in age at UPE, the duration of MV increased 0.65 days (p<0.0001, 95% CI 0.40 to 1.0 day). If an infant had a repeat UPE, the duration of MV increased by 41.3 days (P<0.0001, 23.8 to 58.8 days).

Table 8 Multiple linear regression on duration of mechanical ventilation (n=250)

	Beta Coefficient	**p-value**	**95% confidence interval**
(Constant)	56.788	0.113	-13.452 to 127.028
Weight (grams)	-0.006	0.158	-0.015 to 0.003
Gestational age (weeks)	-0.608	0.534	-2.531 to 1.315
Age at UPE (days)	0.650	**<0.0001**	**0.392 to 0.907**
Did infant have a repeat UPE (yes, no)	41.297	**<0.0001**	**23.806 to 58.787**
Sedation concerns (yes, no)	3.299	0.635	-10.362 to 16.959
Was there loose tapes (yes, no)	-0.312	0.970	-16.690 to 16.066
Original ETT taping protocol (NICU, other)	-11.048	0.212	-28.431 to 6.335

ETT=endotracheal tube; NICU=Neonatal Intensive Care Unit; UPE=unplanned extubation.

The multiple linear regression to predict NICU LOS based on weight, GA, age at UPE, if infant had a repeat UPE, procedures prior to or at UPE, sedation concerns, type of ETT, and ETT taping protocol is found in Table 9. These variables statistically significantly predicted NICU LOS F(8, 232) = 16.942, $p < 0.0001$, $R^2 = 0.369$. Specifically, for every one gram increase in weight, the NICU LOS decreased by 0.01 day or 20.2 minutes (p=0.006, 6 to 30 minutes). For every one day increase in age at UPE, the NICU LOS increased 0.922 days (p<0.0001, 0.7 to 1.2 days). If an infant had a repeat UPE, the NICU LOS increased by 32.7 days (P<0.0001, 15.2 to 50.2 days).

Table 9 Multiple linear regression on NICU LOS (n=241)

	Beta Coefficient	**p-value**	**95% confidence interval**
(Constant)	38.564	0.248	-26.999 to 104.126
Weight (grams)	-0.013	**0.006**	**-0.021 to -0.004**
Gestational age (weeks)	0.405	0.677	-1.509 to 2.319
Age at UPE (days)	0.922	**<0.0001**	**0.668 to 1.176**
Did infant have a repeat UPE (yes, no)	32.706	**<0.0001**	**15.248 to 50.163**
Sedation concerns (yes, no)	6.722	0.329	-6.817 to 20.261
Original ETT taping protocol (NICU, other)	-11.094	0.218	-28.806 to 6.619
Procedures prior to or at UPE (yes, no)	8.263	0.230	-5.263 to 21.789
Type of ETT (oral, nasal)	0.944	0.875	-10.867 to 12.755

ETT=endotracheal tube; NICU=Neonatal Intensive Care Unit; UPE=unplanned extubation.

3.5 Discussion

This study described various UPE reduction strategies implemented in the SickKids NICU, and their impact on UPE events. The study used data on n=302 cases of UPE (257 infants), over a 10-year period, between April 2009 to December 2019. The results showed that the strategies implemented were able to bring the UPE rates below set benchmarks. Between 2003 and 2019, the UPE per 100 ventilator days decreased from 2.38 to as low 0.14 after several major implementation strategies (five PDSA cycles).

The study also described various patient characteristics and variables associated with UPEs, and compared outcomes between biological sex. There were no significant differences in outcomes between males and females, except males (n=129, 92%) received the SK NICU taping protocol more frequently compared to females (n=94, 82.5%). There was a bimodal pattern for GA showing a split at approximately 32 weeks, with infants <32 GA having worse outcomes i.e., more repeat UPE, longer duration of MV and NICU LOS. The study sample had n=45 (12%) repeats in 31 infants, and found worse outcomes compared to infants that only had one UPE. The exploratory analyses showed some trends in infants who had (compared to not) receiving procedures prior to or at the UPE, had sedation concerns, were restrained, received the SK NICU ETT taping protocol, had excessive secretions, and orally intubated (compared to nasal).

3.5.1 SickKids NICU UPE implementation reduction strategies and their impacts

The SickKids NICU had implemented various UPE reduction strategies since 2007, including establishing UPE reduction targets and strategies that were evaluated annually. The following sections describe the strategies SickKids had implemented and how the findings are comparable with other studies.

<u>ETT Holder Trail</u>

The first strategy implemented was a 6-month trial with an ETT holder, conducted in 2007. This strategy did not have a significant impact on the NICU's UPE rate (1.92 to 1.82 to 2.33 per 100 ventilator days). Similar results were observed by Loganathan et al. (2017) (1) who conducted a pre-post study between October 2011 and December 2013 comparing UPE rates with the ETT holder NeoBar® and previous taping methods, in a tertiary NICU in western Canada. During the pre-NeoBar® period (October 2011 to September 2012) 28 UPEs were observed, and during NeoBar® period (January to December 2013) 27 UPEs were observed. This equated to a slight decrease in UPE from 1.47 to 1.17 per 100 ventilator days, but there was no significant difference between time periods. Aydon et al. (2018) (2) conducted an audit to capture UPE data between August 2015 and February 2016 to identify the factors affecting NICU UPEs. The study enrolled 182 neonates among which 41 neonates experienced a UPE. Sixteen of these infants had their ETTs secured using tape, and 25 using the NeoBar® ETT holder. Unfortunately, this study had large amounts of missing information due to poor documentation of UPE events. In addition, these studies had small sample sizes, and were completed over a relatively short duration of time. It is likely the ETT holder did not have a significant impact on reducing UPEs at SickKids because it was used in isolation. Previous literature had shown multiple or bundled interventions were more successful, with one being a standardized approach to ETT securement.(3, 4)

Interdisciplinary Team Formation to Reduce UPEs

In 2008, the SickKids NICU created and implemented strategies to reduce UPEs during a time when there was little guidance in the literature, or from groups such as Society for Airway Management and the Patient Safety Movement Foundation(5). Prior research has shown that many of the SickKids NICU overarching and specific strategies have successfully reduced UPE. First, was the creation of the RUE interdisciplinary Team that included a formal mandate, and routine meetings. A phased-in approach was used by the RUE Team, starting with an environmental scan to understand UPEs and associated gaps in the NICU. This was followed by a literature review that informed the development of specific strategies to reduce UPEs, using a formal QI framework (PDSA). These strategies were put into practice for six-months prior to an initial evaluation, and followed by five PDSA evaluative cycles. The PDSA cycle model has been widely used as part of QI initiatives for several healthcare topics(6). The first phase ("plan") included quantification and benchmarking of UPEs as well as identifying the factors causing UPEs (using a five-year retrospective review of demographic and clinical information on neonates that required MV). The second phase ("do") included implementation of the education program and designing a protocol for weaning. The third phase ("study") included evaluation of the data trend, and the fourth phase ("act") included evaluation of the strategies and sharing the results with clinical providers. Fontánez-Nieves et al. (2016) (7) utilized a PDSA cycle where various strategies to secure ETTs was implemented (loose tape was identified as an important factor causing UPEs). The study observed a 72% decrease in UPE rates (16.1 to 4.5 UPEs per 100 ventilation days) between 2012 and 2014. The effectiveness of the PDSA cycle was also observed in the study conducted by Powell et al. (2016) (8) where a survey was conducted among nurses and RTs to identify the causes of UPEs. This survey informed strategies to correct ETT securing methods, and to standardize ETT positions during procedures such as radiation therapy. The study found UPE rates decreased from 3.8 to 2.7 per 100 ventilation days.

Staff Awareness and Education

There were several key components that were integrated alongside the UPE reduction strategies. These included initial and continuing education using various formats e.g., orientation, education days, simulation, mock codes. The importance of staff education and training were found in many studies. Hewitt et al. (2015) (9) conducted a study to examine the effectiveness of an education-based QI initiative aimed at all NICU staff, in order to decrease the UPE rate. After six months of implementation, the UPE rates decreased from 3.28 to 1.45 per 100 ventilations days. It was also observed that rates of re-intubation following a UPE event decreased from 78.3% to 50%. Similar success for education was observed by a study conducted by Merkel et al. (2014)(10), looking at the impact of UPE reduction strategy bundles. They observed significant decreases in UPE rates (from 2.4 to 0.6 UPEs per 100 ventilator days) between the baseline year of 2009 and the last PDSA cycle in 2013. Interestingly, during the study in 2011, commercially available ETT holders were introduced and resulted in increased rates of UPE (from 1.4 to 1.8 UPEs per 100 ventilator days) because of the lack of familiarity with these devices. As a result of this, the authors introduced real-time analysis of UPE rates along with a process to develop and reinforce staff education, especially with changes in policies or treatments.

Staff Communication

Communication and sharing accountability were key components of success throughout the SickKids UPE reduction implementation processes. This included routine meetings with quality management teams, and safety rounds. In addition, if a UPE event occurred, bedside huddles were conducted with the patient’s care team, including the caregiver. Regular communication (emails, rounds) not only reminded everyone of the actual strategies, but also stressed the importance of a safe learning environment and to celebrate successes. Prior studies have shown inefficient communication among health care professionals is one of the leading causes of medical errors and medical harms (11, 12). Dingley et al. (2008)(13) conducted a study to assess the effectiveness of a comprehensive provider/team communication strategy in an adult medical centre. The authors implemented a structured communication tool, a standardized escalation process to facilitate timely communication, daily multidisciplinary patient-centered rounds using a daily goals sheet, and team huddles during each shift. The study was conducted for 24 months and 495 communications events were analyzed. The results showed a decrease in treatment time, increased nurse satisfaction with communication, and better resolution of patient issues. Panagos et al. (2017) (14) described various factors to make a NICU safer and more reliable in a narrative literature review. In order to have a safer culture, key factors included psychological safety (standardized reporting), accountability, teamwork, and communication (and negotiation) between all levels of hierarchy. These approaches were used by Crezee et al. (2017) (3) when implementing their UPE reduction strategies in a level 4 NICU. Between January 2013 and December 2014 the number of UPEs decreased by 64% (46 to 21), after standardizing practices, ensuring accurate documentation and tracking, and education. The keys to success were accomplished through improved teamwork, accountability, and communication.

Process Standardization

The SickKids NICU developed various tools to help standardize practices. This included reminders such as checklists, signage, and dedicated documentation forms. Routine assessment of ETT security was required twice a shift, and mandatory reporting and documentation incorporated (safety reporting compliance was at 100%). Crezee et al. (2017) (3) conducted a study to observe the effectiveness of multi-step strategies including: 1) at least two care providers at the bedside for the movement of intubated patients, 2) standardizing head and ETT position, 3) establishing a set methodology for ETT security, (4) improved post operative communication, and 5) a post-UPE assessment tool. This resulted in a 50% decrease in monthly UPE events (from 3.8 to 1.9 per month). The UPE events per 100 ventilator days before implementation (2013) decreased by 53% compared to after implementation (2014), from 1.15 to 0.54 UPE per 100 ventilator days. Similarly, Hu et al. (2017) (4) conducted a three-phased standardized evidence-based strategy study that included: 1) stakeholder engagement, 2) implementation of best practice (standard care documentation, standard care implementation, and staff education), and 3) follow-up. They found a reduction in UPE rates from 2.3 to 0.36 per 100 ventilator days. In addition, there was an increase in compliance for standardized care practice documentation (0% to 100%), for standard care practice implementation (0% to 54.9%); and for staff education around ETT (66.7% to 100%).

The UPE reduction mechanisms put in place in the NICU were eventually incorporated into the unit's practice culture, and not only had institutional support, but was also in line with the hospital's patient safety program. The specific UPE reduction strategies implemented have also been evaluated in prior studies. For example, a standardized NICU ETT taping method was instituted as part of the initial set of strategies. This method was amended based on trends and common themes from all PDSA cycles. Loughead et al. (2008) (15) conducted a retrospective cohort study in Central Dupage Hospital in Wheaton, Illinois assessing different taping techniques. They reviewed medical records of all hospitalized infants who received MV between 2002 and 2007, to understand factors associated with NICU UPEs, as well as to help inform practices to reduce UPEs. During this time two strategies were implemented to reduce loose tape related UPEs: consistent taping techniques, and umbilical clamping the ETT. They observed overall reduction of UPE rates, from 4.8 to 0.9 UPEs/100 ventilator days over the 5.5 years. The authors noted that a standardized ETT securement technique helped reduce UPE, but only when associated with full interdisciplinary team participation, adequate education, standard data collection and tracking, including caregiver input, and reinforcing best evidence based practice.

Another notable strategy in the SickKids NICU was having two people involved with procedures (one holding the ETT and the other performing the procedure). Over time, specific roles and procedures were also included e.g., an RT had to be present during a chest X-ray, the inclusion of caregiver input for kangaroo care. Barrosse et al. (2019) (16) developed and implemented similar strategies to standardize ETT management processes in order to reduce UPEs in the NICU. As UPE events mostly occurred during chest x-ray, the study implemented a "holding the ETT during an x-ray" strategy, with the goal to achieve between 48% and 70% compliance and a UPE rate less than 1 per 100 ventilator days. In order to attain the target, strategies included daily ETT audits, decreasing ETT manipulations, increasing education and awareness, and co-ordinating multidisciplinary care. The strategies were successful, as compliance increased from 48% to 91% in a four-month period between October 2018 and February 2019. The study also observed increased awareness among staffs, showing an increase (79% to 100%) in documenting location of ETT during x-ray. The resultant UPE rate was close to their target at 1.2 out of 100 ventilator days.

The Society for Airway Management and the Patient Safety Movement Foundation is a multi-disciplinary group of medical societies, patient safety and QI organizations, whose mandate is to reduce the incidence of UPE, and thus prevent harm and death (17). In order to do this they recommend hospitals take the following three actions (17): 1) take inventory and do an assessment to determine the hospital's rate of UPE. This will help set targets for improvement; 2) collaborate with the local quality and safety teams to increase awareness of UPE and provide the resources for QI initiatives; and 3) develop a QI initiative. The SickKids NICU has undertaken all three of these actions, since 2007. Starting in 2008 with the creation of their RUE Team, through five PDSA cycles, and resulting in a reduction in UPE rate well beyond the initial 50% from 3.0 to as low as 0.14 per 100 ventilator days (and continue to strive for lower and lower targets).

3.5.2 Characteristics of UPEs

This study sample contained a total of 302 infant data who experienced at least one UPE event and among those 45 (12%) were repeated UPE events. Patients who had multiple UPEs had significantly lower birth weight and GA, had less sedation concerns, and were more nasally intubated (than orally intubated), compared to those who had only one UPE. Infant who had multiple UPEs also had longer duration of MV, and LOS. There is a paucity of literature regarding the impact of repeated UPEs in the NICU. Pavlek et al. (2021) (18) conducted a cohort study on neonates who experienced a UPE in a 5-year period, to understand repeated UPE events, short-term complications, as well as long-term morbidities. The authors reviewed 588 events in a tertiary NICU Unit involving 300 patients. One hundred and thirty-three infants (44% of UPEs) experienced at least two UPEs, and 167 infants (56% of all UPEs) experienced one UPE. The group with greater than one UPE was found to have lower median GA at birth (similar to our research) and PMA at the time of the UPE. This group was also found to have a greater number of ETT days (similar to our study), and experienced short-term adverse events compared to the group with only one UPE. As patients experiencing more than one UPE were intubated longer, Pavlek et al. (2021) (18) found a higher risk of airway and pulmonary morbidities. These infants were also observed to have higher odds of tracheostomy and home oxygen or ventilator use. Infants experiencing more than one UPE should be provided extra care to reduce other adverse effects. At SickKids, infants that had more than one UPE were immediately flagged as a high-risk airway. It is likely this strategy, and the "AIRWAY" signage, significantly reduced the risk of further UPE. Only 12% of UPEs in the NICU were repeats, where as Pavlek et al. (2021) observed 44%, and Hewitt et al. (2015) (9) 50% repeat UPEs. Additionally, the "AIRWAY" flag was subsequently implemented throughout the rest of the SickKids institution.

The majority of infants in this study (75%) had procedures prior to, or at the time of UPE. The most common "procedure" was self extubation (coughed our pulled out, n=61, 24%). Previous literature (19) has identified self-extubation as a common cause of UPE in critically ill adults ranging between 64 to 95%. For example one study by Ayllón Garrido et al. (2009) (20) found 73.3% of UPEs occurred due to self-extubation. However, this 6-month study considered only 79 ICU adult patients and observed only 15 UPEs among which 11 UPEs occurred (73%) due to self-extubations. We found few studies describing self-extubation in the neonatal population, each showing different results. Franck et al. (1992) (21) conducted a three month study to understand the reasons for UPEs in a Level 3 NICU. The authors observed 38 UPEs (out of 111 total extubations), with the majority due to self-extubation (23, 62%). This is similar to Ferraz et al. (2019) (22), in a pre-post UPE reduction intervention study, which found a "spontaneous" cause of UPE occurred in 30% (pre) to 50% (post) of the time. However, this is different to Barrose et al. (2019) (16), who found (prior to their QI initiative), 16% of UPEs (out of 44 infants) were "unwitnessed".

It is likely our self extubation number was underestimated because more than 25% of UPEs had no documented procedure associated with the event; it is probable some of these events were self-extubations. In addition, our definition of procedures or circumstances associated wit UPEs may be different than others. For example, Barrosse et al. (2019) considered "patient specific" (21% of UPEs), different from "unwitnessed" causes of UPE; some self extubations may have occurred under the former category. This may be applicable to other procedures as well, as our study included 12 specific items, that may be aggregated under broader categories in other studies. In addition, physical restraints, reintubation, and localized painful stimuli have been found as common causes of self-extubation(23). These could have been factors in our study as n=57 (22%), n=31 (12%), and n=63 (25%) of infants were restrained, re-intubated, and/or had sedation concerns, respectively. Our exploratory analyses revealed that infants with no reported sedation concerns (compared to those with) had significantly less self-extubations. Consistent definitions and/or detailed descriptions of the circumstances or causes associated with UPEs are recommended in future implementations and research.

3.5.3 Comparison Across Sex

In this study, there were very few differences in the outcomes assessed, between males (44%) and females (55%) that had a UPE. Based on the literatures (2, 24), we hypothesized that male infants would experience more UPEs, and worse outcomes compared to female infants. The only significant difference found was the original taping protocol, with more males (n=129, 92%) compared to females (n=94, 83%) receiving the NICU taping protocol compared to other techniques, p=0.03.

There have been a few studies conducted that compared extubation characteristics between male and female infants in the NICU, and we could not find literature comparing different taping techniques between biological sex. Aydon et al. (2018) (2) conducted an audit to capture UPE data in a NICU between August 2015 and February 2016. Out of a total of 224 episodes of ventilation 114 were in male and 68 in female infants. Male infants also had three times the incidence of UPE compared to female infants, with n=31 (76%) and n=10 (24%) respectively. This study did not compare UPE characteristics between biological sexes. Similar findings was also observed by Razavi et al. (2013) (24) who conducted a retrospective cohort study comparing 59 patients who had a UPE in the PICU, with 180 matched controls. A multivariate regression analysis found the odds ratio (OR) for UPE in male infant was 2.53 (95% CI of 1.35-4.23, p=0.005) compared to 0.67 (95% CI of 0.55-1.48, p=0.71) for female infants. In contrast, a retrospective cohort study conducted by Mhanna et al. (2017)(25) investigated a respiratory severity score as a predictor for extubation readiness for VLBW infants. During the study period (2009-2012), 45 out of 147 infants (31%) failed extubation, where n=9 (20%) were UPEs (13 out of 102 [13%] infants successfully extubated were due to UPE). This study did not find any statistical differences between extubation success and failure between biological sexes, and did not delineate between planned and unplanned UPEs.

Prior evidence appeared to indicate male infants may be at higher risk of experiencing a UPE compared to females, but our study showed no difference once the UPE occurred. In this study, we could find little explanation for the difference in taping technique between males and females. There appeared to be more males receiving the NICU taping protocol during the earlier fiscal years (from 2009 to 2014, n=79 males; from 2014 to 2019, n=50 males). In the earlier fiscal years, infants who were transferred to the neighboring hospital NICU would not be re-taped if their tube was believed to be secured for travel (this practice subsequently changed). Razvi et al. (2013)(24) suggested that females may have less secretions, as estrogen may serve as a regulator of secretions from tracheal cells. It is probable males had more secretions compared to females during the earlier fiscal years, thus prompting the RT to re-tape the ETT using the NICU taping protocol. However, this should be taken with caution given our study showed no differences in excessive secretions between males and females, and the study on tracheal cells cited by Razvi et al. (2013)(24) came from a 1989 study by Zeitlin et al. (26) investigating steroid hormones in rabbits.

3.5.4 Gestational Age

This study identified a bimodal pattern for GA, showing a split at approximately 32 weeks. Notable findings in our analysis showed infants less than 32 weeks GA (compare to ≥ 32 weeks), had significantly lower weight, less sedation concerns, less restraint use, more incidence of loose tape and more repeat UPEs. It is possible this younger cohort were not as active or agitated, prompting less use of restraints, and less concerns regarding sedation management. These infants may not have been monitored rigorously, especially given the higher incidence of loose tapes. Given infants less than 32 weeks GA had a higher number of repeat UPEs, it is not surprising they also had significantly longer durations of MV and lengths of NICU stay. It is likely this was influenced by the actual age of the infant at the UPE (and to a lesser extent, birth weight), especially given younger and smaller infants have shorter tracheas (larger impacts with small movements). These variables were significant predictors of duration of MV and length of NICU stay in the multiple linear regression analysis, while GA was not (increasing age and birth weight reduced durations).

Like biological sex, we could not find studies that compared outcomes between GA groups within an exclusive UPE cohort, or studies collecting data on age at UPE. Prior literatures have shown conflicting results with respect to GA and risk of UPEs. da Silva et al. (2013) (27) did a comprehensive review of existing NICU UPE related studies and was not able to draw clear conclusions on whether GA significantly increased UPE risk. It included a pre-post study conducted by Ligi et al. (2010)(28) to identify the effectiveness of patient-safety initiatives (implemented for two years). The main outcome was severe iatrogenic events that included UPE. Most iatrogenic events decreased, however the rate of UPE increased from 5.6 to 15.5 per 1000 ventilator days after the intervention (n=10 pre, n=27 post). Although there was a difference in GA between the two epochs (median 34 weeks pre, 35 weeks post, p=0.015), they attributed the increase to changes in taping technique, and high turnover of caregivers. Veldman et al. (2006) conducted a retrospective study that included 12 UPE incidents in 10 infants (out of 104 ventilated). They found no difference in GA between the 10 infants that experienced a UPE (median 31.5 weeks) and the whole cohort ventilated (32.7 weeks, which included the n=10 UPE infants). The infants that did experience a UPE had significantly longer NICU LOS, and duration of ventilation compared to the whole cohort. With respect to age at UPE, Hatch et al. (2017) (29) in a prospective cohort study of ventilated infants in a level 4 NICU compared infants that had a UPE (n=637) to those who did (n=81). They found daily risk of UPE was significantly associated with age, decreasing until day 7, then increasing after day 7. This aligns with our study as our cohort were a median (IQR) 16.0 (5.0 -38.0) days at the UPE.

Based on the studies above, the influence of GA on clinical outcomes for infants that experience a UPE is unknown. None of the authors did a comparison of outcomes within the UPE cohort based on GA, or chronological age, likely because the sample sizes were very small. Our study included n=257 infants, which enabled us to observe a truer representation of the distribution of UPEs based on GA. We believe UPE incidence follows a bimodal pattern based on GA, with "spikes" below and above 32 weeks. Future investigations should consider assessing exclusive UPE cohorts with larger sample sizes, either in a meta-analysis or as part of a registry. In addition, to further understand risk for UPE, prospective comparisons of our UPE cohort could be made with a matched control group of infants who had planned extubations.

3.5.5 Other Exploratory Analyses

Infants that had sedation concerns (in comparison to those that did not), had higher weight, higher GA, more routine assessments procedures prior to the UPE, and more restraint use. Unlike the findings we found in infants with lower GA, these infants may have been more active, resulting in the higher use of restraints and sedation issues, especially during procedures. A higher proportion of infants with sedation concerns also received the SK NICU taping protocol. Given this taping protocol was standardized and improved throughout the five PDSA cycles, and prior research by Loughead et al. (2008)(15) and Barrosse et al. (2019)(16) on standardized taping techniques also showed reduction in UPEs (previously described), it is not surprising this group also had significantly less loose tapes, less repeat UPEs, lower duration of MV and NICU LOS. Like other topics previously described, there are both limited and conflicting evidence with respect to sedation and physical restraints and UPE. The review by da Silva et al. (2013)(27) found two studies that reported no association between UPE incidence and use of sedatives, while two others found higher incidence of UPE in patients not sufficiently sedated. They also found two studies using limb restraints did not differ between infants that did or did not have a UPE, while another two other studies showed restraints helped prevent UPE. In our study reports of sedation or restraint concerns were low, n=63 (25%) and n=57 (22%), respectively. This is because the NICU balanced the risks associated with UPE, with the risks of sedation and restraint use on neonatal neurodevelopment (30-

33). In fact, use of sedation and restraints were never included as part of RUE implementation strategies because other strategies had greater impacts on UPE rates (and mitigated the risks). Bertoni et al. (2020) (34) in a QI study used similar strategies to enhance neurodevelopmental outcomes while preventing UPEs. They specifically sought to minimize the use of sedation and restraints and encourage skin-to-skin care. After an initial increase in UPEs (like our experience), their rates of UPE showed a decrease from 3.26 to 2.03 UPEs per 100 ventilator days (2015 to 2017), and continue as they progress through further PDSA cycles.

This study showed the proportion of infants intubated orally (n=130, 51%) was fairly even with those with nasal ETTs (n=116, 45%). The exploratory analyses found infants younger at the UPE were orally intubated (compared to nasal). In addition, oral ETT was associated with lower number of repeat UPEs and NICU LOS. There has been very few research conducted on the type of ETT and its impact on neonatal outcome UPEs. A Cochrane review by Spence et al. (2000)(35) investigating complications associated with nasal and oral intubation for neonates, only found two randomized trials, and observed no significant differences in rates of UPE, malposition of the tube, tube blockage, or re-intubation(35) between oral and nasal ETT. Potential disadvantages of the nasal route, in one study showed higher intubation failure rate (n=91), and another showed more frequent post extubation atelectasis (n=86) in infants less than 1500 grams. Our study suggests the oral ETT route may be better than nasal with respect to UPE morbidity, and is likely because infants nasally intubated had more repeat UPEs (n=21, 18% versus n=10, 8%). In our regression analyses ETT type did not have significant impact on NICU LOS, while repeat UPE did.

3.6 Strengths, Limitations and Future Research

This study considers 12 years (2007-2019) of SickKids UPE data in the NICU, providing an understanding of the long-term effectiveness of the various implementation strategies with a fairly large sample. Prior studies investigating this topic were conducted for short to medium durations (one to five years)(3, 4, 7, 8, 15, 16, 36, 37), and none compared outcomes in an exclusive UPE cohort. Future research could investigate how UPE reduction strategies used in the SickKids NICU fit with implementation science frameworks (38-40) to guide other units and/or institutions when establishing their own strategies. This can be accomplished using a qualitative or mixed method approach and including all NICU documentation (e.g., RUE Team meeting minutes, safety reports), focus groups and/or interviewing relevant stakeholders, including caregivers.

To the best of our knowledge, there was no study that compared the UPEs between biological sex. Very few studies have been conducted that differentiate male and female for any NICU related outcomes. This study contributes to the knowledge gap, showing no significant differences between males and females with respect to UPE morbidity. This study did not assess the impact of ethnicity on UPE outcomes, because there were no consistent definitions used in the SickKids NICUs. Since we could not find studies addressing this issue, future studies should be conducted to understand whether ethnicity impacts UPEs for NICU infants.

The study dataset consisted of infants who experienced at least one UPE event. There was no comparison group of infants that did not experience a UPE. Future research could include a prospective comparisons group, matched for key characteristics such as GA, sex, and/or weight (same epoch). This could help determine which reduction strategies made the biggest impact at preventing UPEs in the NICU.

Another limitation of this study was its retrospective design (41). Retrospective studies often have selection bias, information bias and recall bias. In this study selection bias might not have been an issue because it included all available cases of UPE (with no control group). However, information bias could be present because of inconsistent documentation and definitions. For example, “procedure prior to UPE” was categorized in many different subgroups such as self extubation, handling-holding-repositioning, patient transfer, re-taping, tube insertion, diagnostic imaging, suctioning, routine assessment, and bathing. While recording the data, one RT may have interpreted “re-taping” as “routine assessment”, while others described it as “re-taping”. Similarly, RTs may have interpreted UPE events differently e.g., some may have labelled the cause of a

UPE as “agitation”, while others “self-extubation”. Our “self-extubation” numbers may have been underestimated, especially since 25% of the “procedure prior to UPE” information was not recorded. Finally, some of the hard copy blue sheets had large amounts of information, while others had few details (it is likely details were documented in formal safety reports, and/or during oral huddles or rounds). Despite these potential limitations, it is likely information bias was minimized because staff and caregivers in the SickKids NICU were provided extensive education and training on UPE reduction processes. In order to reduce possible biases in future implementation strategies and research, it is recommended that standard definitions for UPE and UPE cause be used, as well as consistent documentation and instructions.

We ran several different subgroup analyses, which may have caused biases related to multiple statistical tests, and diluting of sample sizes. We ran these statistical tests for exploratory purposes only, given the past literature, and availability of the data; inferences from these analyses should be taken with caution. Future research may consider the trends found in our analyses, for explicit investigations such as impact of sedation, restraints, and ETT taping.

Finally, this study was completed in a large tertiary care NICU, which admits a unique mix of pre-term, post-term, and term infants with surgical congenital or acquired anomalies, neurological conditions, and other morbidities. The strategies and characteristics may not be representative of other institutions with mechanically ventilated infants.

3.7 Conclusion

Detailed and well planned UPE reduction strategies implemented over a 12-year period in the SickKids NICU significantly reduced the rate of UPEs. Key factors of success included setting achievable goals, standardization of care practices and documentation (including extensive evaluation), education, integrating processes in the NICU culture, support from all stakeholders, and good communication.

To our knowledge this is the first investigation of a large exclusive UPE cohort (n=257). More males received the SK NICU ETT taping protocol compared to females. Since there were no other differences in outcomes or in the UPE characteristics (and in the literature), it is not clear why this might have occurred. The incidence of UPE occurred in a bimodal pattern, highest for those <32 and ≥ 32 weeks GA. Infants ≥ 32 (compared to <32 weeks) were older when the UPE occurred, had more sedation concerns, and greater use of restraints likely because their maturity allowed for greater activity. Infants with repeat UPE had significantly longer duration of MV and NICU LOS, while those older at the UPE were associated with a reduction in these outcomes.

Future research should explore implementation strategies in more detail using established frameworks, including all available documentation, and interviews with relevant stakeholders. In addition, studies purposefully investigating factors associated with UPE are recommended, with either multi-site data, registries (for larger sample size), and/or prospective designs. This will help other healthcare facilities as well as researchers to inform the development of their own implementation framework to reduce UPEs, and improve patient outcomes.

3.8 References

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Chapter 4. Thesis Conclusions

Mechanical ventilation (MV) is a life supporting treatment to help patients when they are unable to breathe by themselves. Extubations are considered successful when weaning and removal of the endotracheal tube (ETT) from MV are performed as per the medical team's plan. Unplanned extubation (UPE), is the premature or unintended removal of an artificial airway (ETT, tracheostomy tube) by the patient, caregiver or staff (1, 2). UPEs can cause serious adverse events, including hemodynamic instability, increased sepsis risk, increased duration of MV, and NICU length of stay, and complications from re-intubation (higher risk for cardiopulmonary resuscitation, tracheostomy, death) (2-4).

After conducting a comprehensive literature review it was observed that various types of UPE reduction strategies were implemented by many healthcare organizations and researchers including strategies focusing on ETT management (5, 6), evidence-based solutions (1, 7), staff-education (8), and Plan-Do-Study-Act (PDSA) cycles (9-11). Strategies that included multiple interventions (5, 7, 9), accurate data collection and documentation (5, 10), limited nursing workload and patient-to-nurse ratios (7), standardized procedures (6), and improved team communications (11, 12) resulted in improved rates of UPE. It was also found that specific strategies were successful in some studies, while not successful in other studies. The studies (13-16) where strategies did not statistically reduce UPE rates mostly did not account for other risk factors such as patient characteristics and health provider education, which were potentially confounded by policy changes in the hospital. Through the literature review, many knowledge gaps were identified.

Various risk factors and patient characteristics associated with UPEs for NICU infants have been identified in prior research. Patient characteristics such as gestation age (GA) (16), birth weight (BW) (17, 18), and age of patient at UPE (19) have been associated with UPEs. Other factors included self-extubation (20, 21), patient movement (10), patient sedation (22, 23), physical restraint (24, 25), type of ETT (26), history of previous UPE (27), and length of MV (28). However, the impact of these variables varied widely across different studies, some showing increased risk, no risk, or decreased risk of UPE.

The objectives of this study were to:

1. Describe the implementation strategies used to reduce UPE in the SickKids NICU, and their influence on UPE rates in the SickKids NICU.
2. Describe contributing factors and patient characteristics of infants who had a UPE and compare them between biological sex. We hypothesized that male infants experience a higher number of UPEs, and worse outcomes, compared to female infants.

From 2007 to 2019 UPE reduction strategies implemented in the SickKids NICU were successful at reducing UPE below set targets. UPE rates decreased from 2.38 to as low as 0.14 per 100 ventilator days. Key factors of success included setting achievable goals, ensuring strategies were evaluated, amending or developing strategies in response to trends, maintaining consistency with the strategies continuously over the long-term, incorporating it as part of the NICU culture, institutional support and validation, promoting good and honest communication, and sharing the successes. In addition, educational blitzes were routinely organized to refresh staff, and re-iterate the importance of safety reporting; stressing it is not a punitive or “shame and blame” tool but one that highlights system issues, organizes solutions to minimize risk to the patient, and provides a safe environment.

In this study, the only significant difference found between sex was the original taping protocol, with more males (92%) compared to females (83%) receiving the NICU taping protocol compared to other techniques. Males may have had more secretions compared to females during the earlier fiscal years, thus prompting the RT to re-tape the ETT using the NICU taping protocol. However, this is only speculation, and not supported in the literature. The study also identified a bimodal pattern for GA showing a split at approximately 32 weeks. Infants ≥32 weeks GA (compared to <32 weeks) were likely more active because they had significantly higher weight, were older when the UPE occurred, had more sedation concerns, and greater use of restraints. However, they may have been more closely monitored as they had less repeat UPEs, less incidence of loose tapes, and less had the NICU taping protocol (resulting in lower duration of MV and NICU LOS).

Infants who had multiple UPEs were not common (n=31 out of 257), and had significantly lower weight and GA, along with more nasal ETT use, and less concerns about sedation. These infants however, had worse morbidity, with longer duration of MV, and stayed longer in NICU. In order to ameliorate this, the SickKids NICU placed infants with more than one UPE on “high alert”, through various communications, and bedside signage (a strategy implemented by the rest of the hospital).

The most common procedures prior to UPE were self extubations (24%) followed by infant handling or re-positioning (17%). Some procedures or circumstances may have been missed, given about 25% of UPEs had no documented cause associated with them. Consistent definitions and/or detailed descriptions of UPEs are recommended in future.

Infants that had sedation concerns (in comparison to those that did not), had higher weight, higher GA, more routine assessments (prior to the UPE), and more restraint use. These larger and more mature infants may have been more active, resulting in the higher use of restraints and sedation issues, especially during procedures. Reports of sedation or restraint concerns were low (25% and 22% respectively) because the NICU balanced the risks associated with UPE, with the risks of sedation and restraint use on infant neurodevelopment. Use of sedation and restraints were never included as part of RUE implementation strategies because other strategies had greater impact on UPE rates (and mitigating the risks).

This study showed the proportion of infants intubated orally was fairly even with those with nasal ETTs. Our study suggests the oral ETT route may be better than nasal with respect to UPE morbidity (NICU LOS), but is likely because infants nasally intubated had more repeat UPEs. In our regression analyses ETT type did not have significant impact on NICU LOS, while repeat UPE did.

This study is one of the only to investigate a large, and exclusive UPE cohort over a longer time period. Although many of the analyses were exploratory in nature, this study fills in a knowledge gap about UPE characteristics and associations with infant morbidity. The strategies implemented by SickKids were effective at reducing UPEs partly because of the specific and standardized criteria, but mostly because of the global changes in communication, policy, and culture in the NICU. These strategies and processes serve as a useful model for other healthcare facilities and researchers, not just for reducing UPEs, but other practice areas. Assessing success should be planned over the long term as any practice change requires time. Success from the SickKids NICU strategies are evident because they are viewed over a decade. They continue to set new targets, and make innovative changes to UPE reduction strategies in response to trends.

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Appendices

Appendix A: Letters of Research Ethics Board Approval

Ontario Tech University Research Ethics Board

Approval Notice - REB File #16110

researchethics@uoit.ca

Thu 2020-10-22 12:16

To:Mika Nonoyama <Mika.Nonoyama@ontariotechu.ca>;

Cc:researchethics@uoit.ca <researchethics@uoit.ca>;

[EXTERNAL EMAIL]

Date:	*October 22, 2020*
To:	*Mika Nonoyama*
From:	*Paul Yielder, REB Vice-Chair*
File # & Title:	*16110 - Strategies used to Reduce Unplanned Extubations in the Neonatal Intensive Care Unit at SickKids: Ten years of Success*
Status:	***APPROVED***
REB Expiry Date:	***October 01, 2021***

Documents Approved:

SickKids data collection form (after download from REDCap) (Received October 15, 2020)
SickKids REB approved protocol ***(Received October 15, 2020)***
SickKids Amendment approval letter ***(Received October 15, 2020)***
SickKids Amendment application ***(Received October 15, 2020)***
Original SickKids REB application ***(Received October 15, 2020)***
Confidentiality agreement template (Received October 13, 2020)
REB study approval letter from SickKids ***(Received October 13, 2020)***
Data collection template ***(Received October 13, 2020)***
The PI's "TCPS2:CORE" completion certificate ***(Received October 13, 2020)***

Notwithstanding this approval, you are required to obtain/submit, to Ontario Tech Research Ethics Board, any relevant approvals/permissions required, prior to commencement of this project.

The Ontario Tech Research Ethics Board (REB) has reviewed and approved the research study named above to ensure compliance with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2 2018), the Ontario Tech Research Ethics Policy and Procedures and associated regulations. As the Principal Investigator (PI), you are required to adhere to the research protocol described in the REB application as last reviewed and approved by the REB. In addition, you are responsible for obtaining any further approvals that might be required to complete your project.

Under the TCPS2 2018, the PI is responsible for complying with the continuing research ethics reviews requirements listed below:

Renewal Request Form: All approved projects are subject to an annual renewal process. Projects must be renewed or closed by the expiry date indicated above ("Current Expiry"). Projects not renewed 30 days post expiry date will be automatically suspended by the REB; projects not renewed 60 days post expiry date will be automatically closed by the REB. Once your file has been formally closed, a new submission will be required to open a new file.

Change Request Form: If the research plan, methods, and/or recruitment methods should change, please submit a change request application to the REB for review and approval prior to implementing the changes.

Adverse or Unexpected Events Form: Events must be reported to the REB within 72 hours after the event occurred with an indication of how these events affect (in the view of the Principal Investigator) the safety of the participants and the continuation of the protocol (i.e. un-anticipated or un-mitigated physical, social or psychological harm to a participant).

Research Project Completion Form: This form must be completed when the research study is concluded.

Always quote your REB file number (**16110**) on future correspondence. We wish you success with your study.

Sincerely,

Dr. Paul Yielder REB Vice-Chair paul.yielder@uoit.ca	Emma Markoff Research Ethics Assistant researchethics@uoit.ca

NOTE: If you are a student researcher, your supervisor has been copied on this message.

Letter of Approval from the SickKids Research Ethics Board

SickKids

Research Ethics Board (REB)
Study Approval Letter

2019-12-19

Mika Nonoyama
Respiratory Therapy

REB number: 1000066879
Study Title: Strategies used to Reduce Unplanned Extubations in the Neonatal Intensive Care Unit at SickKids: Ten years of Success

Date of Approval: 2019-12-19
Expiry Date: 2020-12-19

Thank you for the application submitted on **2019-11-19**. The above referenced study was reviewed through a delegated process (not by Full Board review). Any concerns arising from this review have been documented and resolved.

The REB voted to approve this study, and your participation as Principal Investigator, as it is found to comply with relevant research ethics guidelines, as well as the Ontario Personal Health Information Protection Act (PHIPA), 2004.

The Hospital for Sick Children Research Ethics Board hereby issues approval for the above named study. This approval is effective from **2019-12-19** to **2020-12-19**. Continuation beyond that date will require further review of REB approval.

The following documents have been reviewed and are approved:

1. Research Protocol, Version Dated November 28, 2019 [Protocol REB NICU UPE 28Nov2019 CLEAN.docx (1.0)]
2. Data Collection Form, Version Dated December 6, 2019 [Data Collection Form PDF UPE 06Dec2019.pdf (1.0)]

The following documents have been reviewed and acknowledged:

1. Master Linking Log, Version Dated October 16, 2019 [Coded Identifier List NICU UPE.xlsx (1.0)]
2. Blue Form, Undated [Blue Form SickKids NICU UPE.pdf (1.0)]

During the course of this investigation, any significant deviations from the approved protocol and/or unanticipated developments or significant adverse events should immediately be brought to the attention of the REB.

Arbelle Manicat-Emo
Vice-Chair, REB

555 University Avenue, Toronto, ON M5G 1X8
Tel: (416) 813-8279 Fax: (416) 813-6515

SickKids

The SickKids REB operates in compliance with the Tri-Council Policy Statement; ICH Guideline for Good Clinical Practice E6(R1); Ontario Personal Health Information Protection Act (2004); Part C Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations and the Medical Devices Regulations of Health Canada. The approval and the views of the REB have been documented in writing. The REB has reviewed and approved the clinical trial protocol and informed consent form for the trial. All investigational drug trials at SickKids are conducted by qualified investigators.

Furthermore, members of the Research Ethics Board who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

Appendix B: Exploratory Analyses Tables

Table A1 UPE Characteristics: Repeat UPE

Variable	Yes Repeat UPEs (n=31)	No Repeat UPEs (n=226)	p-value
Weight (grams) Mean (SD), Median (IQR)	1,525.7 (984.5), 1,065.0 (906.0-2,040.3)	2,199.6 (1,185.4), 2,138.0 (1,149.8-3,059.2)	0.003
Gestational age (weeks) Mean (SD), Median (IQR)	28.0 (4.5), 27.0 (24.0-3.0)	31.2 (5.8), 30.0 (26.0-37.0)	0.003
Age at UPE (days) Mean (SD), Median (IQR)	27.8 (26.9) 19.0 (7.0-45.0)	26.1 (30.7) 15.0 (5.0-38.0)	0.423
Duration of mechanical ventilation (days) Mean (SD), Median (IQR)	83.6 (80.8), 69.0 (26.0-125.0)	33.1 (44.1), 13.0 (4.0-52.0)	<0.0001
Length of stay in NICU Mean (SD), Median (IQR)	95.2 (65.7), 90.2 (38.6-137.3)	50.2 (50.1), 31.6 (11.9-75.2)	<0.0001
Sex, N(%)			0.474
• Male	• 19 (61)	• 122 (55)	
• Female	• 12 (39)	• 102 (46)	
Sedation concerns, N(%)	3 (10)	60 (27)	0.041
Infants GA 32 weeks and older, N(%)	7 (23)	105 (47)	0.01
Patient restrained, N(%)	7 (23)	50 (22)	0.954
Was there loose tape, N(%)	5 (16)	31 (14)	0.717
Presence of excess secretions, N(%)	6 (19)	36 (16)	0.629
Procedures prior to/at UPE occurrence, N(%)			0.067
• Yes	• 12 (39)	• 53 (24)	
• No	• 19 (61)	• 173 (77)	
Type of ETT, N(%)			0.014
• Oral	• 10 (32)	• 120 (56)	
• Nasal	• 21 (68)	• 95 (44)	
Original ETT taping protocol, N(%)			0.097
• NICU taping protocol	• 30 (96.8)	• 195 (86.3)	
• Other taping technique	• 1 (3.2)	• 31 (13.7)	

ETT=Endotracheal Tube; GA=gestational age; IQR=interquartile range; NICU=Neonatal Intensive Care Unit; SD=standard deviation; UPE=Unplanned Extubation.

Table A2 UPE Characteristics: Procedures Prior to UPE

Variable	Yes Procedures (n=65)	No Procedures (n=192)	p-value
Weight (grams) Mean (SD), Median (IQR)	1,857.7 (1,036.3), 1,615.5 (1,000.0-2,392.2)	2,206.7 (1,218.1), 2,160.3 (1,091.0-3,060.0)	0.040
Gestational age (weeks) Mean (SD), Median (IQR)	29.8 (5.5), 28.0 (25.0- 34.0)	31.2 (5.8), 30.0 (26.0-37.0)	0.089
Age at UPE (days) Mean (SD), Median (IQR)	25.9 (25.5) 16.0 (7.0-42.0)	26.4 (31.7) 16.0 (5.0-38.0)	0.599
Duration of mechanical ventilation (days) Mean (SD), Median (IQR)	44.4 (53.8), 22.0 (6.0-59.0)	37.5 (52.1), 15.0 (5.0-52.0)	0.300
Length of stay in NICU Mean (SD), Median (IQR)	68.2 (59.5), 57.8 (18.5-100.0)	51.3 (51.6), 35.5 (12.8-73.2)	0.028
Infants GA 32 weeks and older, N(%)	23 (35)	89(47)	0.101
Sex, N(%)			0.986
• Male	• 36 (55)	• 105 (55)	
• Female	• 29 (45)	• 85 (45)	
Number of UPEs Mean (SD), Median (IQR)	1.3 (0.7), 1.0 (1.0-1.0)	1.1 (0.5), 1.0 (1.0-1.0)	0.064
Repeat UPE, N(%)	12 (19)	19 (10)	0.067
Sedation concerns, N(%)	11 (17)	52 (27)	0.100
Patient restrained, N(%)	15 (23)	42 (22)	0.840
Was there loose tape, N(%)	8 (12)	28 (15)	0.648
Presence of excess secretions, N(%)	7 (11)	35 (18)	0.160
Type of ETT, N(%)			0.001
• Oral	• 20 (34)	• 110 (59)	
• Nasal	• 39 (66)	• 77 (41)	
Original ETT taping protocol, N(%)			0.635
• NICU taping protocol	• 58 (89.2)	• 167 (87.0)	
• Other taping technique	• 7 (10.8)	• 25 (13.0)	

ETT=Endotracheal Tube; GA=gestational age; IQR=interquartile range; NICU=Neonatal Intensive Care Unit; SD=standard deviation; UPE=Unplanned Extubation.

Table A3 UPE Characteristics: Sedation

Variable	Yes Sedation Concerns (n=63)	No Sedation Concerns (n=194)	p-value
Weight (grams) Mean (SD), Median (IQR)	2,520.8 (1,095.1), 2,492.5 (1,538.5-3,191.3)	1,987.6 (1,182.1), 1,770.2 (943.1-2,863.5)	0.002
Gestational age (weeks) Mean (SD), Median (IQR)	33.1 (5.8), 35.0 (28.0-38.0)	30.1 (5.5), 28.0 (25.0-35.0)	0.000
Age at UPE (days) Mean (SD), Median (IQR)	26.4 (40.9) 9.0 (4.0-33.0)	26.2 (26.0) 17.0 (7.0-39.0)	0.137
Duration of mechanical ventilation (days) Mean (SD), Median (IQR)	29.6 (56.8), 11.0 (3.0- 28.0)	42.4 (50.9), 23.0 (5.0- 68.0)	0.010
Length of stay in NICU Mean (SD), Median (IQR)	42.6 (51.9), 21.3 (10.8- 50.4)	59.9 (54.3), 47.4 (15.5- 86.8)	0.007
Infants GA 32 weeks and older, N(%)	39 (63)	73 (38)	0.001
Sex			0.592
• Male, N(%)	• 33 (52)	• 108(56)	
• Female, N(%)	• 30 (48)	• 84(44)	
Number of UPEs Mean (SD), Median (IQR)	1.1 (0.4), 1.0 (1.0-1.0)	1.2 (0.6), 1.0 (1.0-1.0)	0.043
Repeat UPE, N(%)	3 (5)	28 (14)	0.041
Patient restrained, N(%)	24 (38)	33 (17)	0.000
Was there loose tape, N(%)	2 (3)	34 (18)	0.004
Presence of excess secretions, N(%)	11 (18)	31 (16)	0.782
Procedures prior to/at UPE occurrence, N(%)			0.100
• Yes	• 11 (18)	• 54 (28)	
• No	• 52 (83)	• 140 (72)	
Type of ETT, N(%)			0.821
• Oral	• 33 (54)	• 97 (52)	
• Nasal	• 28 (46)	• 88 (48)	
Original ETT taping protocol, N(%)			0.344
• NICU taping protocol	• 53 (84.1)	• 172 (88.7)	
• Other taping technique	• 10 (15.9)	• 22 (11.3)	

ETT=Endotracheal Tube; GA=gestational age; IQR=interquartile range; NICU=Neonatal Intensive Care Unit; SD=standard deviation; UPE=Unplanned Extubation.

Table A4 UPE Characteristics: Patients Restrained

Variable	Yes Restrained (n=57)	No Restrained (n=200)	p-value
Weight (grams) Mean (SD), Median (IQR)	2,595.2 (1,117.7), 2,552.4 (1,875.8-3,156.8)	1,980.0 (1,166.6), 1,661.8 (958.50-2,862.5)	0.001
Gestational age (weeks) Mean (SD), Median (IQR)	32.3 (5.9), 34 (26.0-37.0)	30.4 (5.6), 29.0 (26.0-36.0)	0.025
Age at UPE (days) Mean (SD), Median (IQR)	34.2 (45.2) 16.0 (5.0-49.0)	24.0 (24.0) 16.0 (5.0-36.0)	0.437
Duration of mechanical ventilation (days) Mean (SD), Median (IQR)	29.8 (40.3), 15.0 (4.0-37.0)	42.0 (55.4), 18.5 (5.0-61.5)	0.198
Length of stay in NICU Mean (SD), Median (IQR)	48.4 (53.2), 27.0 (11.7- 59.5)	57.7 (54.4), 41.5 (13.2-84.8)	0.177
Infants GA 32 weeks and older, N(%)	34 (60)	78(40)	0.007
Sex, N(%)			0.876
• Male	• 31 (54)	• 110 (56)	
• Female	• 26 (46)	• 88 (44)	
Number of UPEs Mean (SD), Median (IQR)	1.2 (0.5), 1.0 (1.0-1.0)	1.2 (0.5), 1.0 (1.0-1.0)	0.957
Repeat UPE, N(%)	7 (12)	24 (12)	0.954
Sedation concerns, N(%)	24 (42)	39 (20)	0.000
Was there loose tape, N(%)	5 (9)	31 (16)	0.197
Presence of excess secretions, N(%)	12 (21)	30 (15)	0.276
Procedures prior to/at UPE occurrence, N(%)			0.840
• Yes	• 15 (26)	• 50 (25)	
• No	• 42 (74)	• 150 (75)	
Type of ETT, N(%)			0.635
• Oral	• 27 (50)	• 103 (54)	
• Nasal	• 27 (50)	• 89 (46)	
Original ETT taping protocol, N(%)			**0.020**
• NICU taping protocol	• 55 (96.5)	• 170 (85.0)	
• Other taping technique	• 2 (3.5)	• 30 (15.0)	

ETT=Endotracheal Tube; GA=gestational age; IQR=interquartile range; NICU=Neonatal Intensive Care Unit; SD=standard deviation; UPE=Unplanned Extubation.

Table A5 UPE Characteristics: Loose Tapes

Variable	Yes Lose Tapes (n=36)	No Lose Tapes (n=221)	p-value
Weight (grams) Mean (SD), Median (IQR)	1,778.8 (1,131.4), 1,603.5 (833.0-2,585.4)	2,173.0 (1,183.2), 2,044.8 (1,129.7-3,030.9)	0.064
Gestational age (weeks) Mean (SD), Median (IQR)	28.9(4.7), 27.0 (25.5-31.3)	31.1 (5.8), 30.0 (26.0-36.9)	0.027
Age at UPE (days) Mean (SD), Median (IQR)	32.3 (27.1) 19.0 (11.5-58.5)	25.3 (30.7) 15.0 (5.0-36.0)	0.050
Duration of mechanical ventilation (days) Mean (SD), Median (IQR)	48.3 (49.8), 39.0 (9.5-76.0)	37.8 (53.0), 15.0 (5.0-53.0)	0.044
Length of stay in NICU Mean (SD), Median (IQR)	67.2 (58.7), 55.4 (18.1-88.9)	53.7 (53.3), 37.1 (13.1-78.9)	0.128
Infants GA 32 weeks and older, N(%)	9 (25)	103 (47)	0.013
Sex, N(%)			0.491
• Male	• 18 (50)	• 123 (56)	
• Female	• 18 (50)	• 96 (43)	
Number of UPEs Mean (SD), Median (IQR)	1.2 (0.5), 1.0 (1.0-1.0)	1.2 (0.6), 1.0 (1.0-1.0)	0.707
Repeat UPE, N(%)	5 (14)	26 (12)	0.717
Sedation concerns, N(%)	2 (6)	61 (28)	0.004
Patient restrained, N(%)	5 (14)	52 (24)	0.197
Presence of excess secretions, N(%)	6 (17)	36 (16)	0.955
Procedures prior to/at UPE occurrence, N(%)			0.648
• Yes	• 8 (22)	• 57 (26)	
• No	• 28 (78)	• 164 (74)	
Type of ETT, N(%)			0.197
• Oral	• 14 (42)	• 116 (55)	
• Nasal	• 19 (58)	• 97 (46)	
Original ETT taping protocol, N(%)			0.793
• NICU taping protocol	• 32 (88.9)	• 193 (87.5)	
• Other taping technique	• 4 (11.1)	• 28 (12.7)	

ETT=Endotracheal Tube; GA=gestational age; IQR=interquartile range; NICU=Neonatal Intensive Care Unit; SD=standard deviation; UPE=Unplanned Extubation.

Table A6 UPE Characteristics: Type of ETT

Variable	Oral ETT (n=130)	Nasal ETT (n=116)	p-value
Weight (grams) Mean (SD), Median (IQR)	2,114.1 (1,180.6), 2,023.1 (960.1-3,035.0)	2,167.1 (1,212.8), 2,015.3 (1,143.4-3,026.8)	0.732
Gestational age (weeks) Mean (SD), Median (IQR)	31.4 (5.9), 31.5 (26.0-37.0)	30.4 (5.6), 28.0 (26.0-36.0)	0.187
Age at UPE (days) Mean (SD), Median (IQR)	22.5 (32.8) 11.0 (5.0-29.0)	29.8 (27.3) 19.0 (7.0-49.0)	0.002
Duration of mechanical ventilation (days) Mean (SD), Median (IQR)	36.1 (56.4), 11.5 (4.0-52.0)	40.7 (48.3), 23.5 (7.0-57.0)	0.051
Length of stay in NICU Mean (SD), Median (IQR)	49.0 (55.5), 24.4 (9.9-70.7)	61.6 (52.6), 48.8 (18.3-90.2)	0.003
Infants GA 32 weeks and older, N(%)	64 (50)	45(39)	0.089
Sex, N(%)			0.424
• Male	• 75 (58)	• 61 (53)	
• Female	• 54 (42)	• 54 (47)	
Number of UPEs Mean (SD), Median (IQR)	1.1 (0.4), 1.0 (1.0-1.0)	1.3 (0.7), 1.0 (1.0-1.0)	0.013
Repeat UPE, N(%)	10 (8)	21 (18)	0.014
Sedation concerns, N(%)	33 (25)	28 (34)	0.821
Patient restrained, N(%)	27 (50)	27 (50)	0.635
Was there loose tape, N(%)	14 (11)	19 (16)	0.197
Presence of excess secretions, N(%)	20 (15)	21 (18)	0.568
Procedures prior to/at UPE occurrence, N(%)			0.001
• Yes	• 20 (15)	• 39 (34)	
• No	• 110 (85)	• 77 (66)	
Original ETT taping protocol, N(%)			**0.045**
• NICU taping protocol	• 109 (83.8)	• 107 (92.2)	
• Other taping technique	• 21 (16.2)	• 9 (7.8)	

ETT=Endotracheal Tube; GA=gestational age; IQR=interquartile range; NICU=Neonatal Intensive Care Unit; SD=standard deviation; UPE=Unplanned Extubation.

Table A7 UPE Characteristics: Taping Protocol

Variable	NICU Taping Protocol (n=225)	Other Taping Protocol (n=32)	p-value
Weight (grams) Mean (SD), Median (IQR)	N=220, 2,071.9 (1195.6), 1,844.7 (1,014.2-2,966.6)	2,424.6 (1,047.7) 2,455.7 (1,553.9-3,362.1)	**0.088**
Gestational age (weeks) Mean (SD), Median (IQR)	N=222, 30.4 (5.7) 29.0 (25.0-36.0)	33.8 (5.2), 35.5 (28.0-38.0)	**0.002**
Age at UPE (days) Mean (SD), Median (IQR)	N=223, 28.5 (31.0), 17.0 (7.0-41.0)	10.7(18.0), 3.5 (1.0-7.0)	**<0.0001**
Duration of mechanical ventilation (days) Mean (SD), Median (IQR)	N=221, 43.2 (54.5), 21.0 (7.0-61.5)	11.7 (21.9), 4.0 (1.0-7.8)	**<0.0001**
Length of stay in NICU Mean (SD), Median (IQR)	N=223, 60.2 (55.8), 41.9 (16.5-87.6)	23.4 (22.2), 13.4 (8.3-39.0)	**<0.0001**
Infants GA 32 weeks and older, N(%)	90 (40.5)	22 (68.8)	**0.003**
Sex, N(%)			**0.030**
• Male	• 129 (57.8)	• 12 (37.5)	
• Female	• 94 (42.2)	• 20 (62.5)	
Number of UPEs Mean (SD), Median (IQR)	1.2 (0.6), 1.0 (1.0-1.0)	1.0 (0.2), 1.0 (1.0-1.0)	**0.001**
Repeat UPE, N(%)	30 (13.3)	1 (3.1)	0.097
Sedation concerns, N(%)	53 (23.6)	10 (31.2)	0.344
Patient restrained, N(%)	55 (24.4)	2 (6.2)	0.020
Was there loose tape, N(%)	32 (14.2)	4 (12.5)	0.793
Presence of excess secretions, N(%)	39 (17.3)	3 (9.4)	0.255
Procedures prior to/at UPE occurrence, N(%)			0.635
• Yes	• 58 (25.8)	• 7 (21.9)	
• No	• 167 (74.2)	• 25 (78.1)	
Type of ETT, N(%)			**0.045**
• Oral	• 109 (50.5)	• 21 (52.8)	
• Nasal	• 107 (49.5)	• 9 (30.0)	

ETT=Endotracheal Tube; GA=gestational age; IQR=interquartile range; NICU=Neonatal Intensive Care Unit; SD=standard deviation; UPE=Unplanned Extubation.

Table A8 UPE Characteristics: Excessive Secretions

Variable	Yes secretions (n=42)	No secretions (n=215)	p-value
Weight (grams) Mean (SD), Median (IQR)	2,527.7 (1,104.2), 2,538.3 (1,531.8-3,381.6)	2,041.4 (1,182.5) 1,830.0 (1,000.0-2,941.7)	**0.018**
Gestational age (weeks) Mean (SD), Median (IQR)	32.2 (5.9), 32.5 (26.5-38.0)	30.6 (5.7), 29.0 (25.0-36.0)	0.111
Age at UPE (days) Mean (SD), Median (IQR)	32.0 (31.7), 25.0 (6.0-49.0)	25.2 (29.9) 15.5 (5.0-37.00)	0.261
Duration of mechanical ventilation (days) Mean (SD), Median (IQR)	40.6 (65.5), 12.0 (5.0-50.5)	39.0 (49.9) 17.0 (5.0-57.0)	0.642
Length of stay in NICU Mean (SD), Median (IQR)	48.5 (53.8), 24.2 (12.9-57.0)	57.0 (54.2), 41.9 (13.2-83.5)	0.289
Infants GA 32 weeks and older, N(%)	22 (55.0)	90 (42.1)	0.130
Sex, N(%)			0.818
• Male	• 19 (46.3)	• 95 (44.4)	
• Female	• 22 (53.7)	• 119 (55.6)	
Number of UPEs Mean (SD), Median (IQR)	1.3 (0.7), 1.0 (1.0-1.0)	1.2 (0.5) 1.0 (1.0-1.0)	0.571
Repeat UPE, N(%)	6 (14.3)	25 (11.6)	0.629
Sedation concerns, N(%)	11 (26.2)	52 (24.2)	0.782
Patient restrained, N(%)	12 (28.6)	45 (20.9)	0.276
Was there loose tape, N(%)	6 (14.3)	30 (14.0)	0.955
Procedures prior to/at UPE occurrence, N(%)			0.160
• Yes	• 7 (16.7)	• 58 (27.0)	
• No	• 35 (83.3)	• 157 (73.0)	
Type of ETT, N(%)			0.568
• Oral	• 20 (48.8)	• 110 (53.7)	
• Nasal	• 21 (51.2)	• 95 (46.3)	
Original ETT taping protocol, N(%)			0.255
• NICU taping protocol	• 39 (92.9)	• 186 (86.5)	
• Other taping technique	• 3 (7.1)	• 29 (13.5)	

ETT=Endotracheal Tube; GA=gestational age; IQR=interquartile range; NICU=Neonatal Intensive Care Unit; SD=standard deviation; UPE=Unplanned Extubation.

Table A9 Specific Procedures prior to/at UPE occurrence for Subgroups

Procedures prior to/ at UPE occurrence	**Female**	**Male**	**GA ≥32 wks**	**GA <32 wks**	**Yes Repeat UPEs**	**No Repeat UPEs**
None reported	29(25.4)	36(25.5)	23(20.5)	42(29.6)	53(23.5)	12(38.7)
Self extubation	28(24.6)	33(23.4)	33(29.5)	27(19.0)	7 (22.6)	54 (23.9)
Handling, holding, re-positioning	16(14.0)	27(19.1)	13(11.6)	30(21.1)	4 (12.9)	40 (17.7)
Re-taping ETT	8(7.0)	9(6.4)	6(5.4)	11(7.7)	3 (9.7)	14 (6.2)
Patient transfer	7(6.1)	11(7.8)	7(6.2)	11(7.7)	1 (3.2)	17 (7.5)
Diagnostic imaging	4(3.5)	5(3.5)	4(3.6)	5(3.5)	2 (6.5)	7 (3.1)
Tube insertion	6(5.3)	4(2.8)	6(5.4)	4(2.8)	0 (0.0)	10 (4.4)
Routine assessment	3(2.6)	5(3.5)	6(5.4)	2(1.4)	1 (3.2)	8 (3.5)
Suctioning	5(4.4)	4(2.8)	5(4.5)	4(2.8)	1 (3.2)	8 (3.5)
Bathing	4(3.5)	2(1.4)	5(4.5)	1(0.7)	0 (0.0)	6 (2.7)
Blood work	3(2.6)	0(0.0)	2(1.8)	1(0.7)	0 (0.0)	3 (1.3)
Changing linen	1(0.9)	2(1.4)	1(0.9)	2(1.4)	0 (0.0)	3 (1.3)
Changing incubator or bed	0(0.0)	3(2.1)	1(0.9)	2(1.4)	0 (0.0)	3 (1.3)

Procedures prior to/ at UPE occurrence	**Yes Sedation[a]**	**No Sedation[a]**	**Yes Restrained**	**No Restrained**	**NICU Taping**	**Other Taping**
None reported	11(17.5)	54(27.8)	15(26.3)	50(25.0)	58(25.8)	7(21.9)
Self extubation	**23(36.5)**	**38(19.6)**	18 (31.6)	43(21.5)	57(25.3)	4(12.5)
Handling, holding, re-positioning	7(11.1)	37(19.1)	5(8.8)	39(19.5)	41(18.2)	3(9.4)
Re-taping ETT	2(3.2)	15(7.7)	4(7.0)	13(6.5)	14(6.2)	3(9.4)
Patient transfer	3(4.8)	15(7.7)	2(3.5)	16(8.0)	10(4.4)	8(25.0)
Diagnostic imaging	2(3.2)	7(3.6)	2(3.5)	7(3.5)	7(3.1)	2(6.2)
Tube insertion	1(1.6)	9(4.6)	1(1.8)	9(4.5)	9(4.0)	1(3.1)
Routine assessment	**5(7.9)**	**4(2.1)**	3(5.3)	6(3.0)	7(3.1)	2(6.2)
Suctioning	3(4.8)	6(3.1)	1(1.8)	8(4.0)	8(3.6)	1(3.1)

Bathing	2(3.2)	4(2.1)	4(7.0)	2(1.0)	6(2.7)	0
Blood work	1(1.6)	2(1.0)	1(1.8)	2(1.0)	2(0.9)	1(3.1)
Changing linen	1(1.6)	2(1.0)	1(1.8)	2(1.0)	3(1.3)	0
Changing incubator or bed	2(3.2)	1(0.5)	0(0.0)	3(1.5)	3(1.3)	0

Procedures prior to/ at UPE occurrence	Yes Loose Tapes[b]	No Loose Tapes[b]	Yes Secretions	No Secretions	Oral ETT[c]	Nasal ETT[c]
None reported	8(22.2)	57(25.8)	7(16.7)	58(27.0)	**20(15.4)**	**39(33.6)**
Self extubation	5(13.9)	56(25.3)	13(31.0)	48(22.3)	30 (23.1)	29 (25.0)
Handling, holding, re-positioning	6(16.7)	38(17.2)	7(16.7)	37(17.2)	27 (20.8)	16 (13.8)
Re-taping ETT	**10(27.8)**	**7(3.2)**	4(9.5)	13(6.0)	9(6.9)	6(5.2)
Patient transfer	3(8.3)	15(6.8)	3(7.1)	15(7.0)	13(10.0)	5(4.3)
Diagnostic imaging	1(2.8)	8(3.6)	2(4.8)	7(3.3)	6(4.6)	3(2.6)
Tube insertion	1(2.8)	9(4.1)	1(2.4)	9(4.2)	8(6.2)	2(1.7)
Routine assessment	1(2.8)	8(3.6)	1(2.4)	8(3.7)	6(4.6)	3(2.6)
Suctioning	1(2.8)	8(3.6)	1(2.4)	8(3.7)	5(3.8)	4(3.4)
Bathing	0	6(2.7)	2(4.8)	4(1.9)	2(1.5)	4(3.4)
Blood work	0	3(1.4)	0	3(1.4)	2(1.5)	1(0.9)
Changing linen	0	3(1.4)	1(2.4)	2(0.9)	0	3(2.6)
Changing incubator or bed	0	3(1.4)	0	3(1.4)	2(1.5)	1(0.9)

[a]p=0.047, [b]p=0.001, [c]p=0.033. Bolded numbers: significant post-hoc pairwise, p<0.05. Missing information if total N≠257.
ETT=Endotracheal Tube; GA=gestational age; UPE=Unplanned Extubation.

Appendix C: SickKids Librarian Search Criteria and Search Results

Database [Platform] *Searches run April 21, 2020*	**Results**
MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily [OVID] 1946 to April 20, 2020	154
Embase Classic+Embase [OVID] 1947 to 2020 Week 16	279
Cochrane Central Register of Controlled Trials [OVID] March 2020	17
TOTAL	**450**

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to April 20, 2020 Search Strategy:

#	Searches	Results
1	infant/ or exp infant, newborn/	1128318
2	(pediatric* or paediatric* or child* or newborn* or congenital* or infan* or baby or babies or neonat* or pre-term or preterm* or premature birth* or NICU? or PICU?).tw,kf.	2276077
3	or/1-2	2618002
4	Airway Extubation/ and (accidental or unplanned).tw,kf.	99
5	(extubat* adj3 (accidental or unplan*)).tw,kf.	469
6	or/4-5	480
7	3 and 6	201
8	Airway Extubation/ae [Adverse Effects]	259
9	(adverse effect? or adverse event?).tw,kf.	303225
10	Blood Gas Analysis/	21770
11	blood gas.tw,kf.	17496
12	(oxygen adj2 saturation).tw,kf.	26189
13	child mortality/ or infant mortality/ or perinatal mortality/	31363
14	(child* mortalit* or neonat* mortalit* or newborn mortalit* or new born mortalit* or infan* mortalit*).tw,kf.	24362
15	complication?.tw,kf.	964224
16	"Length of Stay"/	86872
17	(hospital stay? or "length of stay?" or stay length? or PICU stay? or NICU stay?).tw,kf.	129742
18	Patient Harm/	153
19	Patient Safety/	19512
20	(patient harm? or patient safety).tw,kf.	31364
21	Respiratory Rate/	2738
22	(respirat* rate? or respirat* frequency or breathing rate? or breathing frequency).tw,kf.	26071
23	Risk Factors/	812244
24	(risk factor? or relative risk?).tw,kf.	644558
25	treatment outcome/	960002

26	Outcome Assessment, Health Care/	71502
27	(outcome? adj3 (assess* or clinical or patient? or treatment or infant? or baby or babies or newborn? or new born? or neonat*)).tw,kf.	539667
28	ventilat* day?.tw,kf.	1738
29	intubat* day?.tw,kf.	79
30	((decreas* or reduc*) adj5 (UE? or UPE? or accidental extubation? or unplanned extubation?)).tw,kf.	422
31	(incidence adj2 (UE? or UPE? or accidental extubation? or unplannd extubation?)).tw,kf.	37
32	(rate? adj5 (UE? or UPE? or accidental extubation? or unplanned extubation?)).tw,kf.	224
33	or/8-32	3463713
34	3 and 6 and 33	168
35	limit 34 to english language	154

Embase Classic+Embase 1947 to 2020 Week 16 Search Strategy:

#	Searches	Results
1	infant/ or baby/ or high risk infant/ or hospitalized infant/ or newborn/	1149813
2	(pediatric* or paediatric* or child* or newborn* or congenital* or infan* or baby or babies or neonat* or pre-term or preterm* or premature birth* or NICU? or PICU?).tw,kw.	3079541
3	or/1-2	3390189
4	extubation/ and (accidental or unplanned).tw,kw.	744
5	(extubat* adj3 (accidental or unplan*)).tw,kw.	787
6	or/4-5	935
7	adverse event/	38063
8	(adverse effect? or adverse event?).tw,kw.	485618
9	blood gas analysis/	22255
10	blood gas.tw,kw.	26043
11	(oxygen adj2 saturation).tw,kw.	41713
12	Childhood Mortality/ or Newborn Mortality/ or Infant Mortality/	48545
13	(child* mortalit* or neonat* mortalit* or newborn mortalit* or new born mortalit* or infan* mortalit*).tw,kw.	26326
14	complication/	214913
15	complications.tw,kw.	1126681
16	"length of stay"/	184635
17	(hospital stay? or "length of stay?" or stay length? or PICU stay? or NICU stay?).tw,kw.	227030
18	Patient Harm/	1750
19	Patient Safety/	112730
20	(patient harm? or patient safety).tw,kw.	46252

21	breathing rate/	40961
22	(respirat* rate? or respirat* frequency or breathing rate? or breathing frequency).tw,kw.	38799
23	risk factor/	1019912
24	(risk factor? or relative risk?).tw,kw.	948962
25	treatment outcome/	844066
26	Outcome assessment/	525949
27	(outcome? adj3 (assess* or clinical or patient? or treatment or infant? or baby or babies or newborn? or new born? or neonat*)).tw,kw.	868805
28	ventilat* day?.tw,kw.	3424
29	intubat* day?.tw,kw.	149
30	((decreas* or reduc*) adj5 (UE? or UPE? or accidental extubation? or unplanned extubation?)).tw,kw.	668
31	(incidence adj2 (UE? or UPE? or accidental extubation? or unplannd extubation?)).tw,kw.	87
32	(rate? adj5 (UE? or UPE? or accidental extubation? or unplanned extubation?)).tw,kw.	398
33	or/7-32	4716316
34	3 and 6 and 33	299
35	limit 34 to english language	279

Cochrane Central Register of Controlled Trials March 2020 Search Strategy:

#	Searches	Results
1	infant/ or exp infant, newborn/	30812
2	(pediatric* or paediatric* or child* or newborn* or congenital* or infan* or baby or babies or neonat* or pre-term or preterm* or premature birth* or NICU? or PICU?).ti,ab.	180368
3	or/1-2	183826
4	Airway Extubation/ and (accidental or unplanned).ti,ab.	6
5	(extubat* adj3 (accidental or unplan*)).ti,ab.	100
6	or/4-5	102
7	Blood Gas Analysis/	1213
8	blood gas.ti,ab.	3218
9	(oxygen adj2 saturation).ti,ab.	8742
10	child mortality/ or infant mortality/	569
11	(child* mortalit* or neonat* mortalit* or newborn mortalit* or new born mortalit* or infan* mortalit*).ti,ab.	1549
12	complication?.ti,ab.	92226
13	"Length of Stay"/	6901
14	(hospital stay? or "length of stay?" or stay length? or PICU stay? or NICU stay?).ti,ab.	27937

15	Patient Harm/	3
16	Patient Safety/	577
17	(patient harm? or patient safety).ti,ab.	1975
18	Respiratory Rate/	254
19	(respirat* rate? or respirat* frequency or breathing rate? or breathing frequency).ti,ab.	6572
20	risk factors/	24785
21	(risk factor? or relative risk?).ti,ab.	55518
22	Treatment Outcome/	129616
23	(outcome? adj3 (assess* or clinical or patient? or treatment or infant? or baby or babies or newborn? or new born? or neonat*)).ti,ab.	146972
24	ventilat* day?.ti,ab.	500
25	intubat* day?.ti,ab.	39
26	((decreas* or reduc*) adj5 (UE? or UPE? or accidental extubation? or unplanned extubation?)).ti,ab.	85
27	(incidence adj2 (UE? or UPE? or accidental extubation? or unplannd extubation?)).ti,ab.	4
28	(rate? adj5 (UE? or UPE? or accidental extubation? or unplanned extubation?)).ti,ab.	42
29	or/7-26	397091
30	3 and 6 and 29	23
31	limit 30 to english language	17