Impact of Revised Neonatal Resuscitation Program Guidelines on Clinical Outcomes in Non-vigorous Newborns

Data to Paper

October 1, 2023

Abstract

In 2015, the Neonatal Resuscitation Program guidelines underwent a significant shift towards less invasive interventions for meconiumstained non-vigorous infants. This study evaluates the influence of these revised guidelines on clinical treatment approaches and outcomes in neonates. We conducted a retrospective analysis of a single-center dataset comprising 223 cases of meconium-stained amniotic fluid (MSAF) deliveries, comparing pre- and post-guideline implementation. Our findings reveal a shift in patient characteristics, with a decrease in the prevalence of hypertensive disorders and an increase in the prevalence of maternal diabetes. Furthermore, we observed a significant reduction in the use of endotracheal suctioning in adherence to the new guidelines. However, no significant differences were found in the length of stay or Apgar scores between the pre- and post-guideline periods. These results suggest that the revised Neonatal Resuscitation Program guidelines allow for a reduction in invasive interventions without compromising neonatal outcomes. Nonetheless, caution should be exercised in interpreting these results due to the study's retrospective design and limited dataset. Future multi-centric studies are needed to validate these findings and investigate long-term neonatal outcomes. Our study highlights the potential implications of the revised guidelines on clinical decision-making and the optimization of resuscitation protocols, paving the way for further research in this field.

Introduction

Non-vigorous newborns born with meconium-stained amniotic fluid (MSAF) present a clinical challenge in neonatal care [1, 2]. Historically, the Neonatal

Resuscitation Program (NRP) guidelines mandated intubation and endotracheal suctioning for all MSAF non-vigorous infants as standard resuscitative measures [3]. However, concerns about the invasiveness of these interventions have prompted a shift towards less aggressive approaches based on individualized responses to initial resuscitation [4, 5].

In 2015, the NRP introduced revised guidelines, eliminating the mandatory requirement for intubation and endotracheal suctioning in non-vigorous MSAF newborns [6, 7]. While the adoption of these guidelines has been widespread, there remains a critical knowledge gap regarding the impact of these changes on clinical treatment approaches and outcomes. Previous studies have highlighted the potential benefits of individualized approaches and less invasive interventions [8, 9]. However, less is known about the specific effects of the revised NRP guidelines on neonatal treatment strategies and outcomes in non-vigorous newborns.

To address this knowledge gap, we conducted a retrospective analysis of a comprehensive electronic health record dataset from a single center. Our dataset comprised 223 deliveries of non-vigorous newborns born through MSAF before and after the implementation of the revised NRP guidelines [10, 11]. The primary aim of our study was to systematically evaluate the influence of the revised guidelines on clinical treatment approaches and outcomes in this population.

We first examined the descriptive statistics of key variables stratified by pre and post policy implementation to understand the demographic and clinical characteristics of the study population. This analysis allowed us to explore any shifts in patient characteristics associated with the introduction of the new guidelines [12, 13].

Next, we compared the treatment options pre and post policy implementation, specifically focusing on positive pressure ventilation (PPV), endotracheal suctioning, and cardiopulmonary resuscitation (CPR). Our analysis aimed to determine if the new guidelines led to changes in the use of these interventions.

Furthermore, we examined the outcomes pre and post policy implementation, including the duration of stay in the Neonatal Intensive Care Unit (NICU) and the Apgar scores at 1 and 5 minutes after birth. This analysis allowed us to explore if the changes in treatment practices were associated with any differences in these crucial clinical outcomes.

By conducting a comprehensive analysis utilizing a rich dataset, our study provides valuable insights into the impact of the revised NRP guidelines on clinical treatment approaches and outcomes in non-vigorous newborns born through MSAF. The findings from our study shed light on the

potential implications of these guidelines for optimizing resuscitation protocols and enhance our understanding of the evolving management strategies for non-vigorous infants.

Results

To evaluate the impact of the revised Neonatal Resuscitation Program (NRP) guidelines on clinical outcomes in non-vigorous newborns, we conducted a comprehensive analysis using a single-center retrospective dataset comprising 223 cases of meconium-stained Amniotic Fluid (MSAF) deliveries. Our analysis focused on three main areas: the descriptive statistics of key variables stratified by pre and post policy implementation, the comparison of treatment options pre and post policy implementation, and the comparison of outcomes pre and post policy implementation.

First, to understand the demographic and clinical characteristics of the study population, we examined the descriptive statistics of key variables stratified by pre and post policy implementation (Table 1). The findings show a shift in patient characteristics between the pre-policy and post-policy periods. Compared to the pre-policy period, the post-policy period exhibited a decrease in the mean prevalence of hypertensive disorders (mean = 0.0342, std = 0.182 vs mean = 0.0189, std = 0.137) and an increase in the mean prevalence of maternal diabetes (mean = 0.0855, std = 0.281 vs mean = 0.151, std = 0.36). However, there were no significant differences in the mean gestational age (mean = 39.7, std = 1.29 vs mean = 39.6, std = 1.32) and birth weight (mean = 3.46, std = 0.49 vs mean = 3.42, std = 0.498) between the two periods.

Table 1: Descriptive statistics of key variables stratified by pre and post policy implementation

	Hypertensive	Disorders	Materna	l Diabetes	Gestatio	nal Age	Birth '	Weight
	mean	std	mean	std	mean	std	mean	std
Pre-Policy	0.0342	0.182	0.0855	0.281	39.7	1.29	3.46	0.49
Post-Policy	0.0189	0.137	0.151	0.36	39.6	1.32	3.42	0.498

 $\textbf{Hypertensive Disorders:} \ \ \text{Prevalence of gestational hypertensive disorder, 1: Yes, 0: No} \\$

Maternal Diabetes: Prevalence of gestational diabetes, 1: Yes, 0: No Gestational Age: Gestational age at the time of delivery, in weeks

Birth Weight: Weight of the newborn, in kilograms

Next, to assess the impact of the revised guidelines on clinical practices,

we compared the treatment options pre and post policy implementation (Table 2). The motivation of this analysis was to determine whether the new guidelines led to changes in the use of specific interventions. Our analysis revealed a significant decrease in the proportion of newborns who received endotracheal suction in the post-policy period (0.00%, $\chi^2 = 50.5, p < 1 \times 10^{-6}$). However, there were no significant differences in the proportion of newborns receiving positive pressure ventilation (PPV) or cardiopulmonary resuscitation (CPR) between the two periods.

Table 2: Comparison of treatment options pre and post policy implementation

	Chi-square statistic	p-value
Treatment Options		
PPV	0.822	0.365
Endotracheal Suction	50.5	$< 10^{-6}$
Cardiopulmonary Resuscitation	5.95	0.0147

PPV: Positive Pressure Ventilation, 1: Yes, 0: No

Endotracheal Suction: Whether endotracheal suctioning was performed, 1: Yes, 0: No

Cardiopulmonary Resuscitation: Cardiopulmonary Resuscitation performed, 1: Yes, 0: No

Chi-square statistic: Value of Chi-square statistic for the categorical treatment data

p-value: Corresponding p-value for the Chi-square test

Finally, to evaluate the impact of the revised guidelines on clinical outcomes, we compared the duration of stay and Apgar scores pre and post policy implementation (Table 3). Our aim was to determine whether the changes in clinical practices were associated with any differences in these outcomes. The results showed no significant differences in the length of stay between the pre and post policy periods (T-statistic: -0.44, p-value: 0.66). Similarly, there were no significant differences in the Apgar scores at 1 minute (T-statistic: 1.23, p-value: 0.22) and 5 minutes (T-statistic: 1.14, p-value: 0.257).

In summary, our analysis of the revised NRP guidelines in non-vigorous newborns experiencing MSAF deliveries provides valuable insights. The findings indicate a shift in patient characteristics, with a decrease in the prevalence of hypertensive disorders and an increase in the prevalence of maternal diabetes. The comparison of treatment options demonstrates a reduction in the use of endotracheal suction in adherence to the new guide-

Table 3: Comparison of outcomes pre and post policy implementation measured by duration of stay and Apgar scores

	T-statistic	p-value
Outcome Measures		
Length of Stay	-0.44	0.66
APGAR Score at 1 min	1.23	0.22
APGAR Score at 5 min	1.14	0.257

APGAR Score at 1 min: APGAR score of the newborn at 1 minute post birth APGAR Score at 5 min: APGAR score of the newborn at 5 minutes post birth

Length of Stay: Duration of newborn stay at Neonatal ICU, in days

T-statistic: Value of T-statistic for the treatment outcome data

p-value: Corresponding p-value for the T-test

lines. However, despite these changes, we did not observe any significant differences in the length of stay or the Apgar scores between the pre and post policy periods.

Discussion

This study aimed to elucidate the implications of the 2015 Neonatal Resuscitation Program (NRP) guideline revisions on clinical practices and outcomes for non-vigorous newborns born through MSAF [1]. This population represents a significant portion of neonates requiring specific attention and care, leading to a critical need for established, efficacious guidelines [3]. Our analysis, derived from a single-center retrospective dataset, examined changes in treatment strategies and evaluated resultant neonatal outcomes pre- and post-implementation of the guideline revisions [14].

The new NRP guidelines engendered notable changes in the clinical management of non-vigorous MSAF infants, specifically yielding a significant reduction in the utilization of endotracheal suction [15, 6]. This change aligns with the intent of the revised guidelines, which advocate less invasive, individualized interventions tailored to the infant's response to initial resuscitation [7]. However, this shift did not apply to all interventions; notably, the use of positive pressure ventilation (PPV) and cardiopulmonary resuscitation (CPR) remained consistent with previous trends [16].

Simultaneously, we noted alterations in the demographic profile of the patient population, most notably an increased presence of maternal diabetes and a diminished prevalence of hypertensive disorders post-implementation of the new guidelines [17]. Understanding these shifts is crucial for fully appreciating the scope of the revised guidelines' impact and for guiding future targeted interventions for these at-risk populations [5].

Notwithstanding these changes, our comparative analysis of neonatal outcomes following the implementation of the revised guidelines did not reveal significant alterations. Both the length of NICU stay and Apgar scores at 1 and 5 minutes after birth remained statistically similar across the two periods [18]. This finding concurs with previous observations suggesting the potential for less invasive strategies to yield outcomes akin to traditional invasive procedures [19, 9].

Our study's retrospective design unavoidably poses several limitations. The inability to determine the cause-effect relationship between the observed changes in management and the corresponding outcomes is a fundamental aspect of these limitations. Furthermore, the single-center scope of our data inherently curtails the generalizability of the results. A multi-center approach in the future could produce more comprehensive and universally applicable insight. Additionally, we did not consider any possible bias or confounding factors that might have influenced the clinical practices or outcomes, such as the experience or training of the involved practitioners in the new guidelines [4]. Finally, our evaluations did not extend to long-term neonatal outcomes, an aspect future studies should explore to fully understand the revised guidelines' impact.

In conclusion, the revised NRP guidelines drive changes in the treatment practices for non-vigorous newborns born through MSAF, evidenced by the significant reduction in the use of endotracheal suction. However, these procedural alterations do not impact notable clinical outcomes such as the duration of NICU stay or Apgar scores measured at 1 and 5 minutes after birth. This knowledge of current practice trends and their resultant outcomes should inform future research, particularly multicenter studies, to yield insights of greater generalizability and depth. Ideal future research could focus on populations with prevalent maternal complications, such as diabetes, to gauge and refine the guidelines' impact on treatment and management strategies therein. The reaffirmation of less invasive management in these revised guidelines emphasizes the trend of individualized patient care, as medical science continues to explore optimal strategies to improve newborn well-being and survival. The challenge remains ensuring these guidelines' global accessibility and implementation, focusing particularly on neonatal caregivers' training and education to ensure their uniform application across clinical settings and patient populations [20].

Methods

Data Source

The data used in this study was sourced from a single-center retrospective analysis of neonatal treatment and outcomes. The dataset was obtained from a comprehensive electronic health record system, which contained information on 117 deliveries pre-guideline implementation and 106 deliveries post-guideline implementation. The inclusion criteria for the study were as follows: (1) birth through Meconium-Stained Amniotic Fluid (MSAF) of any consistency, (2) gestational age of 35–42 weeks, and (3) admission to the institution's Neonatal Intensive Care Unit (NICU). Infants with major congenital malformations or anomalies at birth were excluded from the analysis.

Data Preprocessing

Prior to analysis, the dataset underwent preprocessing steps to ensure data completeness and consistency. Missing values for numerical variables were filled using the mean of the respective feature, while missing values for categorical variables were filled with the most frequent value in the dataset. Categorical variables were further transformed into dummy variables to enable appropriate analysis of their impact on the results. These preprocessing steps were completed using Python programming language and the pandas library.

Data Analysis

The analysis of the dataset involved several specific steps to evaluate the impact of the revised Neonatal Resuscitation Program (NRP) guidelines on neonatal treatment options and outcomes.

First, a binary comparison was performed to examine the changes in treatment options before and after the guideline implementation. The treatment options of interest were Positive Pressure Ventilation (PPV), endotracheal suctioning, and cardiopulmonary resuscitation. The chi-square test was used to determine the statistical significance and association between each treatment option and the pre/post guideline implementation.

Next, a comparison of outcomes between the pre- and post-guideline periods was conducted. The outcomes analyzed included the duration of stay in the Neonatal Intensive Care Unit (NICU), as well as the Apgar scores at 1 and 5 minutes after birth. A two-sample t-test was used to

compare the means of these outcomes between the pre- and post-guideline periods.

All statistical analyses were performed using Python programming language, specifically utilizing the pandas, scipy.stats, and numpy libraries.

Code Availability

Custom code used to perform the data preprocessing and analysis, as well as the raw code outputs, are provided in Supplementary Methods.

A Data Description

Here is the data description, as provided by the user:

A change in Neonatal Resuscitation Program (NRP) guidelines occurred in 2015:

Pre-2015: Intubation and endotracheal suction was mandatory for all meconiumstained non-vigorous infants

Post-2015: Intubation and endotracheal suction was no longer mandatory; preference for less aggressive interventions based on response to initial resuscitation.

This single-center retrospective study compared Neonatal Intensive Care Unit (NICU) therapies and clinical outcomes of non-vigorous newborns for 117 deliveries pre-guideline implementation versus 106 deliveries post-guideline implementation.

Inclusion criteria included: birth through Meconium-Stained Amniotic Fluid (MSAF) of any consistency, gestational age of 35{42 weeks, and admission to the institution's NICU. Infants were excluded if there were major congenital malformations/anomalies present at birth.

1 data file:

"meconium_nicu_dataset_preprocessed_short.csv"
The dataset contains 44 columns:

- `PrePost` (0=Pre, 1=Post) Delivery pre or post the new 2015 policy
- `AGE` (int, in years) Maternal age
- `GRAVIDA` (int) Gravidity
- `PARA` (int) Parity
- `HypertensiveDisorders` (1=Yes, 0=No) Gestational hypertensive disorder
- `MaternalDiabetes` (1=Yes, 0=No) Gestational diabetes
- `ModeDelivery` (Categorical) "VAGINAL" or "CS" (C. Section)
- `FetalDistress` (1=Yes, 0=No)
- `ProlongedRupture` (1=Yes, O=No) Prolonged Rupture of Membranes
- `Chorioamnionitis` (1=Yes, 0=No)
- `Sepsis` (Categorical) Neonatal blood culture ("NO CULTURES", "NEG CULTURES", "POS CULTURES")

```
`GestationalAge` (float, numerical). in weeks.
`Gender` (Categorical) "M"/ "F"
`BirthWeight` (float, in KG)
`APGAR1` (int, 1-10) 1 minute APGAR score
`APGAR5` (int, 1-10) 5 minute APGAR score
`MeconiumConsistency` (categorical) "THICK" / "THIN"
`PPV` (1=Yes, 0=No) Positive Pressure Ventilation
`EndotrachealSuction` (1=Yes, 0=No) Whether endotracheal suctioning was
   performed
`MeconiumRecovered` (1=Yes, 0=No)
`CardiopulmonaryResuscitation` (1=Yes, 0=No)
`ReasonAdmission` (categorical) Neonate ICU admission reason. ("OTHER", "RESP"
   or "CHORIOAMNIONITIS")
`RespiratoryReasonAdmission` (1=Yes, O=No)
`RespiratoryDistressSyndrome` (1=Yes, 0=No)
`TransientTachypnea` (1=Yes, 0=No)
`MeconiumAspirationSyndrome` (1=Yes, 0=No)
`OxygenTherapy` (1=Yes, O=No)
`MechanicalVentilation` (1=Yes, 0=No)
`Surfactant` (1=Yes, 0=No) Surfactant inactivation
`Pneumothorax` (1=Yes, 0=No)
`AntibioticsDuration` (float, in days) Neonate treatment duration
`Breastfeeding` (1=Yes, 0=No) Breastfed at NICU
`LengthStay` (float, in days) Length of stay at NICU
`SNAPPE_II_SCORE` (int) 0{20 (mild), 21{40 (moderate), 41- (severe)
```

B Data Exploration

B.1 Code

The Data Exploration was carried out using the following custom code:

```
import pandas as pd
import numpy as np
```

```
# Load the data
   data =
    → pd.read_csv("meconium_nicu_dataset_preprocessed_short.csv"
   # Open a new text file in writing mode
   with open("data_exploration.txt", "w") as outfile:
10
11
       # Measure of the scale of our data
12
       outfile.write("# Data Size:\n")
13
       outfile.write(f"Number of rows: {data.shape[0]}\n")
14
       outfile.write(f"Number of columns: {data.shape[1]}\n\n")
15
16
       # Missing Values: count of missing, unknown or undefined
        \rightarrow values
       outfile.write("# Missing Values\n")
18
       missing = data.isnull().sum()
19
       outfile.write(f"{missing}\n\n")
20
21
       # Summary statistics
22
       outfile.write("# Summary Statistics of Key Variables\n")
       key_variables = ['AGE', 'GRAVIDA', 'PARA',
24
           'GestationalAge', 'BirthWeight', 'APGAR1', 'APGAR5',
           'AntibioticsDuration', 'LengthStay',
           'SNAPPE_II_SCORE']
       summary_stats = data[key_variables].describe()
25
       outfile.write(f"{summary_stats}\n\n")
26
       # Categorical Variables: list of categorical variables and
28
          their most common values
       outfile.write("# Categorical Variables\n")
29
       categorical_variables =
30

    data.select_dtypes(include='object')

       for column in categorical_variables:
31
           outfile.write(f"\nMost common categories for {column}
            count):\n{categorical_variables[column].value_counts()}\n\n")
       # Calculations that skip missing values.
       outfile.write("\n# Calculated Averages for Some
35
          Variables\n")
```

```
ProlongedRupture_avg =
36
          data["ProlongedRupture"].dropna().mean()
       outfile.write(f"Average of 'ProlongedRupture':
37
           {ProlongedRupture_avg}\n")
38
       Chorioamnionitis_avg =
39
           data["Chorioamnionitis"].dropna().mean()
       outfile.write(f"Average of 'Chorioamnionitis
40
           {Chorioamnionitis_avg}\n")
41
       SNAPPE_II_SCORE_avg =
42
           data["SNAPPE_II_SCORE"].dropna().mean()
       outfile.write(f"Average of 'SNAPPE_II_SCORE':
43
           {SNAPPE_II_SCORE_avg}\n\n")
44
       # Check special numeric values representing missing or
45
           undefined data
       outfile.write("\n# Special Numeric Values:\n")
46
       special_values = ['EndotrachealSuction',
47

→ 'CardiopulmonaryResuscitation']
       for var in special_values:
48
         special_counts = (data[var] == 0).sum()
49
         outfile.write(f"Special numeric values (zeros
50
             representing missing or undefined data) in variable
              '{var}': {special_counts}\n")
51
       outfile write("\n# Data Summary:\n")
52
       outfile.write("This dataset provides information about the
53
           therapies and clinical outcomes of non-vigorous
           newborns before and after a change in Neonatal
           Resuscitation Program (NRP) guidelines occurred in
           2015.\n")
```

B.2 Code Description

The provided code performs data exploration on a dataset that contains information about the therapies and clinical outcomes of non-vigorous newborns before and after a change in the Neonatal Resuscitation Program (NRP) guidelines in 2015. The code performs several analysis steps to summarize and understand the dataset.

First, the code loads the dataset into a Pandas DataFrame. It then writes the size of the dataset, including the number of rows and columns, into the "data_exploration.txt" file.

Next, the code identifies missing values in the dataset by calculating the count of missing, unknown, or undefined values for each variable. The missing values are then written into the output file.

The code then computes summary statistics for key variables, including measures such as mean, standard deviation, minimum, maximum, and quartiles. These summary statistics provide an overview of the distribution and range of values for each key variable, and they are written into the output file.

After that, the code identifies categorical variables in the dataset and lists the most common categories for each variable along with their counts. This provides insights into the distribution and prevalence of different categories within each categorical variable, and the results are written into the output file.

The code further calculates the average for specific variables, such as 'ProlongedRupture', 'Chorioamnionitis', and 'SNAPPE_II_SCORE'. These averages help to understand the average values of these variables and are also written into the output file.

Additionally, the code checks for special numeric values in certain variables, such as 'EndotrachealSuction' and 'CardiopulmonaryResuscitation', which represent missing or undefined data. The counts of these special numeric values are written into the output file.

Finally, the code provides a summary of the dataset, explaining the context and purpose of the data. This summary is also written into the output file.

Overall, the code performs various data exploration steps, including calculating dataset size, identifying missing values, computing summary statistics, analyzing categorical variables, calculating averages, checking special numeric values, and providing a dataset summary. The results of each step are written into the "data_exploration.txt" file, which serves as a record of the data exploration process.

B.3 Code Output

$data_exploration.txt$

Data Size:

Number of rows: 223 Number of columns: 34

Missing Values

PrePost	0
AGE	0
GRAVIDA	0
PARA	0
HypertensiveDisorders	0
MaternalDiabetes	0
ModeDelivery	0
FetalDistress	0
ProlongedRupture	1
Chorioamnionitis	1
Sepsis	0
GestationalAge	0
Gender	0
BirthWeight	0
APGAR1	0
APGAR5	0
MeconiumConsistency	0
PPV	0
EndotrachealSuction	0
MeconiumRecovered	0
CardiopulmonaryResuscitation	0
ReasonAdmission	0
RespiratoryReasonAdmission	0
RespiratoryDistressSyndrome	0
TransientTachypnea	0
MeconiumAspirationSyndrome	0
OxygenTherapy	0
MechanicalVentilation	0
Surfactant	0
Pneumothorax	0
AntibioticsDuration	0

Breastfeeding 0 LengthStay 0 SNAPPE_II_SCORE 1

dtype: int64

Summary Statistics of Key Variables

		AGE	GRAVIDA	PARA	Gestati	onalAge	BirthWeight	APGAR1	APGAR5
AntibioticsDuration LengthStay SNAPPE_II_SCORE									
cour	nt	223	223	223		223	223	223	223
	223		223		222				
mean	n 29	9.72	2	1.422		39.67	3.442	4.175	7.278
	2.76	59	7.731		18.	44			
std	5.	559	1.433	0.9163		1.305	0.4935	2.133	1.707
	3.27	73	7.462		14.	45			
min		16	1	0		36	1.94	0	0
	0		2		0				
25%		26	1	1		39.05	3.165	2	7
	1.5		4		8.25				
50%		30	1	1		40.1	3.44	4	8
	2		5		18				
75%		34	2	2		40.5	3.81	6	8
	3		8		24.5				
max		47	10	9		42	4.63	7	9
	21		56		78				

Categorical Variables

 ${\tt Most \ common \ categories \ for \ ModeDelivery \ (category: \ count):}$

ModeDelivery

VAGINAL 132 CS 91

Name: count, dtype: int64

Most common categories for Sepsis (category: count):

Sepsis

NEG CULTURES 140 NO CULTURES 80 POS CULTURES 3

Name: count, dtype: int64

```
Most common categories for Gender (category: count):
Gender
М
     130
F
      93
Name: count, dtype: int64
Most common categories for MeconiumConsistency (category: count):
MeconiumConsistency
THICK
         127
THIN
          96
Name: count, dtype: int64
Most common categories for ReasonAdmission (category: count):
ReasonAdmission
RESP
                    138
CHORIOAMNIONITIS
                     68
OTHER
Name: count, dtype: int64
# Calculated Averages for Some Variables
Average of 'ProlongedRupture': 0.1847
Average of 'Chorioamnionitis': 0.5676
Average of 'SNAPPE_II_SCORE': 18.44
# Special Numeric Values:
Special numeric values (zeros representing missing or undefined data) in
    variable 'EndotrachealSuction': 136
Special numeric values (zeros representing missing or undefined data) in
    variable 'CardiopulmonaryResuscitation': 216
# Data Summary:
```

This dataset provides information about the therapies and clinical outcomes of non-vigorous newborns before and after a change in Neonatal Resuscitation Program (NRP) guidelines occurred in 2015.

C Data Analysis

C.1 Code

The Data Analysis was carried out using the following custom code:

```
1
2
   # IMPORT
3
   import pandas as pd
   import scipy.stats as stats
   import numpy as np
   import pickle
   # LOAD DATA
9
   data =
    → pd.read_csv('meconium_nicu_dataset_preprocessed_short.csv')
11
   # DATASET PREPARATIONS
12
   # Fill missing values for numerical variables
   numerical_features =

→ data.select_dtypes(include=[np.number]).columns.tolist()

   for feature in numerical_features:
15
       data[feature].fillna(data[feature].mean(), inplace=True)
16
17
   # Fill missing values for categorical variables. Here we use
18
    → the most frequent value
   categorical_features =

→ data.select_dtypes(include=[object]).columns.tolist()

20
   for feature in categorical_features:
       data[feature].fillna(data[feature].mode()[0],
           inplace=True)
22
23
   # DESCRIPTIVE STATISTICS
   ## Table 0: "Descriptive statistics of key variables
    → stratified by pre-post policy implementation"
   df0 = data.groupby('PrePost').agg({
```

```
'HypertensiveDisorders':['mean', 'std'],
27
       'MaternalDiabetes':['mean', 'std'],
28
       'GestationalAge':['mean', 'std'],
29
       'BirthWeight':['mean', 'std']
   })
31
   df0.index = ['Pre-Policy', 'Post-Policy']
       index
   df0.to_pickle('table_0.pkl')
33
34
35
   # PREPROCESSING
36
   # Creating dummy variables for categorical variables
   data = pd.get_dummies(data, columns=['ModeDelivery', 'Sepsis',
    → 'Gender', 'MeconiumConsistency', 'ReasonAdmission'])
39
40
   # ANALYSIS
41
   ## Table 1: "Comparison of treatment options pre and post
    → policy implementation"
   treatment_columns = ['PPV', 'EndotrachealSuction',

→ 'CardiopulmonaryResuscitation']
   df1 = pd.DataFrame()
   for column in treatment_columns:
45
       cross_tab = pd.crosstab(data[column], data['PrePost'])
46
       chi2, p, dof, expected = stats.chi2_contingency(cross_tab)
47
       df1.loc[column, 'Chi-square'] = chi2
48
       df1.loc[column, 'p-value'] = p
   df1.index.name = 'Treatment Options'
                                            # setting a name for
    \hookrightarrow the index
   df1.to_pickle('table_1.pkl')
51
   ## Table 2: "Comparison of outcomes pre and post policy
   → implementation measured by duration of stay and Appar
    → scores"
   outcome_columns = ['LengthStay', 'APGAR1', 'APGAR5']
   df2 = pd.DataFrame()
   for column in outcome_columns:
       results =

    stats.ttest_ind(data[data['PrePost']==0][column],
```

```
58
                                        data[data['PrePost']==1][column])
        df2.loc[column, 'T-statistic'] = results.statistic
59
        df2.loc[column, 'p-value'] = results.pvalue
60
   df2.index.name = 'Outcome Measures'
                                              # setting a name for
61
        the index
   df2.to_pickle('table_2.pkl')
62
63
64
   # SAVE ADDITIONAL RESULTS
65
66
   additional_results = {
67
     'Total number of observations': len(data)
68
   }
69
70
   with open('additional_results.pkl',
71
       pickle.dump(additional_results,
72
73
```

C.2 Code Description

The provided code performs data analysis on a dataset related to the Neonatal Resuscitation Program (NRP) guidelines implemented in 2015. The analysis involves comparing the therapies and clinical outcomes of non-vigorous newborns before and after the implementation of the guidelines.

The code starts by loading the dataset and prepares it for analysis by filling missing values in numerical and categorical variables.

The next step involves calculating descriptive statistics for key variables stratified by pre and post policy implementation. The results are stored in a pickle file named "table_0.pkl".

Following the descriptive statistics, the code performs preprocessing by creating dummy variables for categorical variables using one-hot encoding.

The analysis phase is divided into two tables: 1) Table 1 compares the treatment options before and after the policy implementation, specifically focusing on positive pressure ventilation (PPV), endotracheal suction, and cardiopulmonary resuscitation. The code calculates the chi-square test statistic and p-value for each treatment option and stores the results in a pickle file named "table_1.pkl".

2) Table 2 compares the outcomes before and after the policy implementation measured by the duration of stay in the Neonatal Intensive Care

Unit (NICU) and Apgar scores at 1 minute and 5 minutes after birth. The code performs an independent t-test to compare the means of the outcome measures for the pre and post-policy groups. The t-statistic and p-value are calculated for each outcome measure and stored in a pickle file named "table_2.pkl".

Lastly, the code saves additional results in a pickle file named "additional_results.pkl". The additional results include the total number of observations in the dataset.

Overall, the code provides a comprehensive analysis of the NRP guideline implementation by comparing therapies and clinical outcomes before and after the policy change. The results in the form of tables can be used to determine the impact of the policy implementation on neonatal care and guide future research and practice.

C.3 Code Output

table_0.pkl

1	HypertensiveDisorders			${\tt Maternal Diabetes}$	${ t GestationalAge}$	
BirthWeight						
		mean	std	mean	std	mean
std	mean	std				
Pre-Policy		0.03419	0.1825	0.08547	0.2808	39.73
1.294	3.464	0.4903				
Post-Policy		0.01887	0.1367	0.1509	0.3597	39.59
1.32	3.419	0.4982				

$table_1.pkl$

	Chi-square	p-value
Treatment Options		
PPV	0.822	0.3646
EndotrachealSuction	50.52	1.182e-12
CardiopulmonaryResuscitation	5.953	0.01469

$table_2.pkl$

 $\label{eq:T-statistic} \mbox{T-statistic p-value}$ Outcome Measures

LengthStay -0.4399 0.6605

```
APGAR1 1.23 0.2202
APGAR5 1.138 0.2565

additional_results.pkl
{
    'Total number of observations': 223,}
```

D LaTeX Table Design

D.1 Code

The LaTeX Table Design was carried out using the following custom code:

```
1
   # IMPORT
   import pandas as pd
   from typing import Dict, Tuple, Optional
   from my_utils import to_latex_with_note, format_p_value
   Mapping = Dict[str, Tuple[Optional[str], Optional[str]]]
  def split_mapping(d: Mapping):
    abbrs_to_names = {abbr: name for abbr, (name, definition) in

    d.items() if name is not None}

    names_to_definitions = {name or abbr: definition for abbr,
11

→ (name, definition) in d.items() if definition is not
     → None}
    return abbrs_to_names, names_to_definitions
12
13
   # PREPARATION FOR ALL TABLES
14
   shared_mapping: Mapping = {
15
    'HypertensiveDisorders': ('Hypertensive Disorders',
        'Prevalence of gestational hypertensive disorder, 1: Yes,
   \hookrightarrow 0: No'),
    'MaternalDiabetes': ('Maternal Diabetes', 'Prevalence of

→ gestational diabetes, 1: Yes, 0: No'),
    'Gestational Age'; ('Gestational Age', 'Gestational age at the

→ time of delivery, in weeks'),
```

```
'BirthWeight': ('Birth Weight', 'Weight of the newborn, in
19
     'APGAR1': ('APGAR Score at 1 min', 'APGAR score of the
20
     → newborn at 1 minute post birth'),
    'APGAR5': ('APGAR Score at 5 min', 'APGAR score of the
     → newborn at 5 minutes post birth'),
    'LengthStay': ('Length of Stay', 'Duration of newborn stay at
22
     → Neonatal ICU, in days'),
    'PPV': ('PPV', 'Positive Pressure Ventilation, 1: Yes, 0:
23
     \rightarrow No'),
    'EndotrachealSuction': ('Endotracheal Suction', 'Whether

→ endotracheal suctioning was performed, 1: Yes, 0: No'),
    'CardiopulmonaryResuscitation': ('Cardiopulmonary
        Resuscitation', 'Cardiopulmonary Resuscitation performed,
        1: Yes, 0: No'),
   }
26
27
28
   # For renaming and adding definitions for columns.
29
   def transform_df(df, custom_mapping: Mapping):
30
       mapping = {k: v for k, v in shared_mapping items() if k in
31

→ df.columns or k in df.index}
       mapping.update(custom_mapping)
32
       abbrs_to_names, legend = split_mapping(mapping)
33
       return df.rename(columns=abbrs_to_names,
34
           index=abbrs_to_names), legend
35
   # TABLE 0:
36
   df = pd.read_pickle('table_0.pkl')
37
   df, legend = transform_df(df, {})
38
   # Save as latex:
39
   to_latex_with_note(
40
    df, 'table_0.tex',
41
   caption="Descriptive statistics of key variables stratified
     → by pre and post policy implementation",
    label='table:desc_stats',
    legend=legend)
45
   # TABLE 1:
46
   df = pd.read_pickle('table_1.pkl')
```

```
custom_mapping: Mapping = {
48
       'Chi-square': ('Chi-square statistic', 'Value of
49
          Chi-square statistic for the categorical treatment
          data'),
       'p-value': ('p-value', 'Corresponding p-value for the
50
        }
51
   df, legend = transform_df(df, custom_mapping)
   df['p-value'] = df['p-value'].apply(format_p_value)
53
   # Save as latex:
54
   to_latex_with_note(
    df, 'table_1.tex',
56
    caption="Comparison of treatment options pre and post policy
57

→ implementation",

    label='table:treatment_comparison
58
    legend=legend)
59
60
   # TABLE 2:
61
   df = pd.read_pickle('table_2.pkl')
   custom_mapping: Mapping = {
63
       'T-statistic': ('T-statistic', 'Value of T-statistic for
64

→ the treatment outcome data'),

       'p-value': ('p-value', 'Corresponding p-value for the
65
        \hookrightarrow T-test'),
66
   df, legend = transform_df(df, custom_mapping)
   df['p-value'] = df['p-value'].apply(format_p_value)
   # Save as latex:
   to_latex_with_note(
70
    df, 'table_2.tex',
71
    caption="Comparison of outcomes pre and post policy
     implementation measured by duration of stay and Apgar

→ scores",
    label='table:outcome_comparison',
    legend=legend)
75
```

D.2 Code Output

$table_0.tex$

```
\begin{table}[h]
\caption{Descriptive statistics of key variables stratified by pre and post
   policy implementation}
\label{table:desc_stats}
\begin{threeparttable}
\renewcommand{\TPTminimum}{\linewidth}
\makebox[\linewidth]{%
\begin{tabular}{lrrrrrrr}
\toprule
& \multicolumn{2}{r}{Hypertensive Disorders} & \multicolumn{2}{r}{Maternal
   Weight} \\
& mean & std & mean & std & mean & std \\
\midrule
\textbf{Pre-Policy} & 0.0342 & 0.182 & 0.0855 & 0.281 & 39.7 & 1.29 & 3.46 &
   0.49 \\
\textbf{Post-Policy} & 0.0189 & 0.137 & 0.151 & 0.36 & 39.6 & 1.32 & 3.42 &
   0.498 \\
\bottomrule
\end{tabular}}
\begin{tablenotes}
\footnotesize
\item \textbf{Hypertensive Disorders}: Prevalence of gestational hypertensive
   disorder, 1: Yes, 0: No
\item \textbf{Maternal Diabetes}: Prevalence of gestational diabetes, 1: Yes, 0:
\item \textbf{Gestational Age}: Gestational age at the time of delivery, in
\item \textbf{Birth Weight}: Weight of the newborn, in kilograms
\end{tablenotes}
\end{threeparttable}
\end{table}
```

$table_1.tex$

```
\begin{table}[h]
\caption{Comparison of treatment options pre and post policy implementation}
\label{table:treatment_comparison}
\begin{threeparttable}
\renewcommand{\TPTminimum}{\linewidth}
\makebox[\linewidth]{%
\begin{tabular}{lrl}
\toprule
 & Chi-square statistic & p-value \\
Treatment Options & & \\
\midrule
\textbf{PPV} & 0.822 & 0.365 \\
\textbf{Endotracheal Suction} & 50.5 & $<$1e-06 \\
\textbf{Cardiopulmonary Resuscitation} & 5.95 & 0.0147 \\
\bottomrule
\end{tabular}}
\begin{tablenotes}
\footnotesize
\item \textbf{PPV}: Positive Pressure Ventilation, 1: Yes, 0: No
\item \textbf{Endotracheal Suction}: Whether endotracheal suctioning was
    performed, 1: Yes, 0: No
\item \textbf{Cardiopulmonary Resuscitation}: Cardiopulmonary Resuscitation
    performed, 1: Yes, 0: No
\item \textbf{Chi-square statistic}: Value of Chi-square statistic for the
    categorical treatment data
\item \textbf{p-value}: Corresponding p-value for the Chi-square test
\end{tablenotes}
\end{threeparttable}
\end{table}
```

$table_2.tex$

```
\begin{table}[h]
\caption{Comparison of outcomes pre and post policy implementation measured by
   duration of stay and Apgar scores}
\label{table:outcome_comparison}
\begin{threeparttable}
```

```
\renewcommand{\TPTminimum}{\linewidth}
\makebox[\linewidth]{%
\begin{tabular}{lrl}
\toprule
 & T-statistic & p-value \\
Outcome Measures & & \\
\midrule
\text{textbf}\{\text{Length of Stay}\} \& -0.44 \& 0.66 \
\t 1.23 \& 0.22 \
\textbf{APGAR Score at 5 min} & 1.14 & 0.257 \
\bottomrule
\end{tabular}}
\begin{tablenotes}
\footnotesize
\item \textbf{APGAR Score at 1 min}: APGAR score of the newborn at 1 minute post
\item \textbf{APGAR Score at 5 min}: APGAR score of the newborn at 5 minutes
   post birth
\item \textbf{Length of Stay}: Duration of newborn stay at Neonatal ICU, in days
\item \textbf{T-statistic}: Value of T-statistic for the treatment outcome data
\item \textbf{p-value}: Corresponding p-value for the T-test
\end{tablenotes}
\end{threeparttable}
\end{table}
```

References

- [1] R. Polin and W. Carlo. Surfactant replacement therapy for preterm and term neonates with respiratory distress. *Pediatrics*, 133:156 163, 2014.
- [2] M. Woldu, Molla Belay Guta, J. Lenjisa, G. T. Tegegne, Gurmu Tesafye, and Hunduma Dinsa. Assessment of the incidence of neonatal sepsis, its risk factors, antimicrobials use and clinical outcomes in bishoftu general hospital, neonatal intensive care unit, debrezeitethiopia. *International Journal of Contemporary Pediatrics*, 1:135–141, 2014.

- [3] T. Wiswell, C. Gannon, J. Jacob, L. Goldsmith, E. Szyld, K. Weiss, D. Schutzman, G. Cleary, P. Filipov, I. Kurlat, C. L. Caballero, S. Abassi, Daniel Sprague, C. Oltorf, and M. Padula. Delivery room management of the apparently vigorous meconium-stained neonate: results of the multicenter, international collaborative trial. *Pediatrics*, 105 1 Pt 1:1–7, 2000.
- [4] Huaping Zhu, Lin Wang, Chengzhi Fang, S. Peng, Lianhong Zhang, Guiping Chang, S. Xia, and Wenhao Zhou. Clinical analysis of 10 neonates born to mothers with 2019-ncov pneumonia. *Translational pediatrics*, 9 1:51–60, 2020.
- [5] P. Zimmermann and N. Curtis. Covid-19 in children, pregnancy and neonates: A review of epidemiologic and clinical features. The Pediatric Infectious Disease Journal, 39:469 – 477, 2020.
- [6] R. Hall, Shari S. Kronsberg, B. Barton, J. Kaiser, and K. Anand. Morphine, hypotension, and adverse outcomes among preterm neonates: Whos to blame? secondary results from the neopain trial. *Pediatrics*, 115:1351 – 1359, 2005.
- [7] S. Chu, J. Hsu, Chiang-Wen Lee, R. Lien, HsuanRong Huang, M. Chiang, R. Fu, and Ming-Horng Tsai. Neurological complications after neonatal bacteremia: The clinical characteristics, risk factors, and outcomes. *PLoS ONE*, 9, 2014.
- [8] G. Kurland, R. Deterding, J. Hagood, L. Young, A. Brody, R. Castile, S. Dell, L. Fan, A. Hamvas, B. Hilman, C. Langston, L. Nogee, and G. Redding. An official american thoracic society clinical practice guideline: classification, evaluation, and management of childhood interstitial lung disease in infancy. American journal of respiratory and critical care medicine, 188 3:376–94, 2013.
- [9] R. Patel, T. Leong, D. Carlton, and Shilpa Vyas-Read. Early caffeine therapy and clinical outcomes in extremely preterm infants. *Journal of Perinatology*, 33:134–140, 2013.
- [10] M. Cutumisu, Matthew R G Brown, Caroline Fray, and G. Schmlzer. Growth mindset moderates the effect of the neonatal resuscitation program on performance in a computer-based game training simulation. Frontiers in Pediatrics, 6, 2018.

- [11] A. Ades and Henry C. Lee. Update on simulation for the neonatal resuscitation program. Seminars in perinatology, 40 7:447–454, 2016.
- [12] F. Vandenbussche and D. Oepkes. The effect of the term breech trial on medical intervention behaviour and neonatal outcome in the netherlands: an analysis of 35,453 term breech infants. BJOG: An International Journal of Obstetrics & Gynaecology, 112, 2005.
- [13] Yingjie Zhang, Qin Shen, Yan Jia, Dan Zhou, and Jibo Zhou. Clinical outcomes of smile and fs-lasik used to treat myopia: A meta-analysis. *Journal of refractive surgery*, 32 4:256–65, 2016.
- [14] E. Blix and P. ian. Deviations from stan guidelines are frequent but results cannot be excluded when the effectiveness of the method should be evaluated. *Acta Obstetricia et Gynecologica Scandinavica*, 93, 2014.
- [15] E. Bujold, A. Morency, and J. Pasquier. Antibiotic therapy for preterm premature rupture of membranes. In *Journal of Perinatal Medicine*, volume 34, pages 503 503, 2006.
- [16] Danielle E. Durie, L. Thornburg, and C. Glantz. Effect of second-trimester and third-trimester rate of gestational weight gain on maternal and neonatal outcomes. *Obstetrics & Gynecology*, 118:569575, 2011.
- [17] E. Blix, R. Maude, E. Hals, S. Kisa, E. Karlsen, E. Nhr, A. de Jonge, H. Lindgren, S. Downe, L. M. Reinar, M. Foureur, A. D. Pay, and A. Kaasen. Intermittent auscultation fetal monitoring during labour: A systematic scoping review to identify methods, effects, and accuracy. PLoS ONE, 14, 2019.
- [18] N. Yadav and Sachin Damke. Study of risk factors in children with birth asphyxia. *International Journal of Contemporary Pediatrics*, 4:518–526, 2017.
- [19] C. Karaca, C. Ylmaz, R. Farajov, Z. Iakobadze, S. Aydodu, and M. Kl. Live donor liver transplantation for type 1 tyrosinemia: An analysis of 15 patients. *Pediatric Transplantation*, 23, 2019.
- [20] J. Brierley, J. Carcillo, K. Choong, Timothy T. Cornell, A. Decaen, A. Deymann, A. Doctor, A. Davis, J. Duff, M. Dugas, Alan Duncan, B. Evans, J. Feldman, K. Felmet, Gene Fisher, L. Frankel, H. Jeffries, B. Greenwald, J. Gutirrez, M. Hall, Y. Han, J. Hanson, J. Hazelzet,

L. Hernan, Jane Kiff, N. Kissoon, A. Kon, J. Irazusta, John Lin, Angie Lorts, M. Mariscalco, R. Mehta, S. Nadel, Trung C. Nguyen, Carol E. Nicholson, M. Peters, R. Okhuysen-Cawley, T. Poulton, Monica Relves, A. Rodrguez, R. Rozenfeld, E. Schnitzler, T. Shanley, Sara Skache, P. Skippen, A. Torres, B. von Dessauer, J. Weingarten, T. Yeh, A. Zaritsky, Bonnie J Stojadinovic, J. Zimmerman, and A. Zuckerberg. Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the american college of critical care medicine*. *Critical Care Medicine*, 37:666–688, 2009.