Impact of Updated Neonatal Resuscitation Guidelines on Clinical Practices and Outcomes in Non-Vigorous Newborns

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Abstract

Effective resuscitation of non-vigorous newborns is critical for improving neonatal outcomes. However, the impact of updated neonatal resuscitation guidelines on therapies and clinical outcomes in nonvigorous newborns remains uncertain. This study aimed to investigate the association between the updated guidelines and changes in therapies and clinical outcomes in non-vigorous newborns. A retrospective analysis was conducted on a single-center dataset, comparing 117 deliveries before and 106 deliveries after the guideline implementation. The revised guidelines resulted in significant changes in therapies, with a decrease in endotracheal suctioning and an increase in the recovery of meconium. However, these guideline changes did not lead to measurable improvements in neonatal outcomes, as assessed by APGAR scores, length of Neonatal Intensive Care Unit stay, and SNAPPE-II scores. The absence of a significant association between the policy change and neonatal outcomes suggests that factors beyond the changes in the resuscitation guidelines may contribute to the clinical outcomes of non-vigorous newborns. These findings highlight the need for further research to explore the long-term implications and broader implementation of these guidelines in diverse clinical settings.

Introduction

Neonatal resuscitation is a critical procedure that heavily influences the immediate and long-term health outcomes of newborns [1, 2, 3]. The process, which can often be a matter of life or death, is meticulously guided by the recommendations furnished in the Neonatal Resuscitation Program (NRP)

guidelines. These guidelines, subject to periodical revisions to accommodate the most current scientific evidence, underwent notable modifications in 2015, explicitly concerning non-vigorous neonates born through Meconium-Stained Amniotic Fluid (MSAF) [4]. The primary aim of these updates was to improve neonatal outcomes by moving towards less aggressive and more responsive interventions [5, 6]. Nonetheless, the real-world impacts of these amendments on both the therapeutic strategies implemented and the subsequently achieved outcomes, are worth exploring through empirical research [7, 8].

Previous studies have broadened our understanding of the neonatal outcomes linked to the erstwhile and new guidelines and how variable these can be based on specific therapies adopted during the resuscitation process [9, 10]. However, the existing literature does not conclusively determine whether the 2015 updates have actually resulted in improved neonatal outcomes [11, 12]. Addressing this research gap is thus of paramount significance, particularly considering the widespread use of NRP guidelines in clinical settings [13, 14].

Our study attempts to fill this knowledge gap by leveraging a single center retrospective cohort of non-vigorous newborns [15, 16]. By juxtaposing pre and post-2015 guideline implementation outcomes and therapies, this research intends to offer an informed insight into the practical effects of these amendments [17, 18].

Adopting a quantitative research approach, our study exhaustively explores specific neonatal outcomes such as the APGAR score, length of stay, and SNAPPE-II score, which serve as crucial indices of neonatal health [2]. Our statistical analysis also investigates the influence of the new guidelines on NRP therapies, such as endotracheal suctioning and meconium recovery [19, 20]. The findings from this research endeavor will shed light on whether the updates to the guidelines, while shifting clinical practices, have also translated into measurable improvements in neonatal outcomes [21, 22].

Results

In this retrospective single-center study, we aimed to investigate the association between the updated neonatal resuscitation guidelines and changes in therapies and clinical outcomes in non-vigorous newborns. Our analysis revealed significant changes in therapies following the implementation of the updated guidelines. Specifically, as shown in Table 1, there was a significant decrease in the performance of endotracheal suctioning (Chi-

square=50.5, p-value $< 10^{-6}$) and an increase in the recovery of meconium (Chi-square=21.2, p-value= $4.19\ 10^{-6}$). This suggests that the changes in the guidelines led to a shift in clinical practices towards less aggressive interventions for meconium-stained non-vigorous infants.

To examine whether these guideline changes had an impact on neonatal outcomes, we performed linear regression analysis. As shown in Table 2, the regression analysis did not reveal any statistically significant effects of the policy change on the neonatal outcomes. There were no significant associations between the policy change and APGAR1 score (Coefficient=-0.351, p-value=0.22), APGAR5 score (Coefficient=-0.26, p-value=0.257), length of Neonatal Intensive Care Unit (NICU) stay (Coefficient=0.441, p-value=0.66), or SNAPPE-II score (Coefficient=-0.00569, p-value=0.998). These findings indicate that the updated neonatal resuscitation guidelines did not result in measurable improvements in neonatal outcomes.

As summarized in Table 3, we also examined the key variables before and after the implementation of the guideline changes. There were no substantial differences in the average age of the mother, average gestational age, average birth weight, average APGAR1 score, average APGAR5 score, average length of NICU stay, or average SNAPPE-II score between the pre and post-guideline implementation groups. Additionally, the total number of observations in the dataset was 223, as indicated in the additional results.

In summary, our analysis demonstrated that the updated neonatal resuscitation guidelines resulted in significant changes in therapies but did not lead to measurable improvements in neonatal outcomes. The absence of a significant association between the policy change and neonatal outcomes suggests that factors beyond the changes in the resuscitation guidelines may contribute to the clinical outcomes of non-vigorous newborns. These findings highlight the need for further research to explore the long-term implications and broader implementation of these guidelines in diverse clinical settings.

Discussion

This study specifically explores the impact of the 2015 updates in the Neonatal Resuscitation Program (NRP) guidelines on the clinical practices and neonatal outcomes for non-vigorous neonates born through Meconium-Stained Amniotic Fluid (MSAF) [4]. Our study, building on the well-documented significance of neonatal resuscitation for infant health outcomes [1, 3], utilized a single-center retrospective cohort, comprising deliveries before and after the introduction of the policy shift.

In this investigation, a significant shift towards less aggressive interventions was observed, reflected in a decrease in the use of endotracheal suctioning and an increase in meconium recovery [6, 10]. These findings align with prior reports that have documented similar perceptible shifts in clinical practices following major guideline updates [13, 14]. However, our finding of no significant improvements in neonatal outcomes such as APGAR scores, length of stay at NICU, or SNAPPE-II scores post-implementation [23, 24] is consistent with existing literature, thereby reinforcing the narrative of an elusive association between NRP changes and immediate neonatal outcomes [25, 26].

Although our work offers important insights, it has limitations. Firstly, the study relies on a single-center retrospective cohort limiting its potential for generalization. Secondly, the study does not account for data on long-term outcomes of non-vigorous neonates, which could provide a fuller picture of the impact of the 2015 updates [10]. Another limitation is the inability to control for individual provider approaches and the maternal health conditions, both of which can significantly impact neonatal outcomes. Future studies should consider longitudinal designs and multivariate models to address these limitations.

In conclusion, while our research identified noteworthy changes in clinical practices post the 2015 NRP guideline updates, these shifts did not translate into significant improvements in immediate neonatal outcomes. These findings underscore the need for comprehensive strategies that extend beyond guideline updates and account for other potentially influential factors in neonatal care. We hope this will spur further research to explore the long-term impact of such guidelines on non-vigorous neonates and inform potential modifications to the neonatal resuscitation guidelines [6].

Methods

Data Source

The data used in this study were obtained from a single-center retrospective analysis of non-vigorous newborns in a Neonatal Intensive Care Unit. The dataset consisted of 117 deliveries before and 106 deliveries after the implementation of updated neonatal resuscitation guidelines in 2015. The inclusion criteria for the study were birth through Meconium-Stained Amniotic Fluid of any consistency, gestational age of 35–42 weeks, and admission to the institution's Neonatal Intensive Care Unit. Infants with major congenital malformations/anomalies were excluded from the analysis.

Data Preprocessing

The data preprocessing steps were performed using Python programming language. The dataset was loaded into a pandas dataframe for further analysis. No additional preprocessing steps were required as the dataset was already preprocessed and formatted appropriately for analysis.

Data Analysis

The analysis of the dataset was conducted using various statistical techniques in order to investigate the association between the updated neonatal resuscitation guidelines and changes in therapies and clinical outcomes in non-vigorous newborns.

First, descriptive statistics were generated to summarize key variables before and after the implementation of the new policy. Mean values for age, gestational age, birth weight, APGAR scores, length of stay, and SNAPPE-II scores were calculated separately for the pre and post-policy implementation groups.

Next, a series of chi-square tests were performed to assess the association between the change in the new treatment policy and changes in specific therapies. The treatments compared included positive pressure ventilation, endotracheal suctioning, recovery of meconium, cardiopulmonary resuscitation, respiratory related admissions, respiratory distress syndrome, transient tachypnea, meconium aspiration syndrome, oxygen therapy, mechanical ventilation, surfactant administration, and pneumothorax. The results were reported as chi-square values and associated p-values.

Additionally, linear regression analyses were conducted to evaluate the impact of the policy change on neonatal outcomes. The outcomes assessed included APGAR scores, length of stay, and SNAPPE-II scores. Separate regression models were fitted for each outcome variable, with the change in treatment policy as the explanatory variable. The coefficient and p-value associated with the change in treatment policy were reported for each regression model.

All analyses were performed using appropriate statistical packages in Python, and the results were summarized in tables for further interpretation and discussion.

Code Availability

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

Table 1: Association between change in new treatment policy and changes in treatments

	Chi-square	P-value
Treatment		
PPV (Positive Pressure Ventilation)	0.822	0.365
Endotracheal Suction	50.5	$< 10^{-6}$
Meconium Recovered	21.2	$4.19 \ 10^{-6}$
Cardiopulmonary Resuscitation	5.95	0.0147
Reason for Admission - Respiratory	1.16	0.281
Respiratory Distress Syndrome	0.844	0.358
Transient Tachypnea	0.0574	0.811
Meconium Aspiration Syndrome	0.932	0.334
Oxygen Therapy	0	1
Mechanical Ventilation	1.09	0.297
Surfactant	0	1
Pneumothorax	1.18	0.278
Breastfeeding	0.00626	0.937

Chi-square: Chi-square Test Statistic

P-value: Computed P-value

Treatment: Types of Neonatal Treatments

PPV (Positive Pressure Ventilation): Whether positive pressure ventilation was performed, 1:Yes, 0:No

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

Meconium Recovered: Whether Meconium was recovered, 1:Yes, 0:No

Cardiopulmonary Resuscitation: Whether cardiopulmonary resuscitation was performed, 1:Yes, 0:No

Reason for Admission - Respiratory: Admission due to respiratory reason, 1:Yes, 0:No

Respiratory Distress Syndrome: Presence of respiratory distress syndrome, 1:Yes, 0:No

Transient Tachypnea: Presence of transient tachypnea, 1:Yes, 0:No

Meconium Aspiration Syndrome: Presence of meconium aspiration syndrome, 1:Yes, 0:No

Oxygen Therapy: Whether oxygen therapy was given, 1:Yes, 0:No Mechanical Ventilation: Mechanical Ventilation performed, 1:Yes, 0:No

Table 2: Linear regression analysis of impact of policy change on neonatal outcomes

	Coefficient	P-value
Outcome		
APGAR1 Score	-0.351	0.22
APGAR5 Score	-0.26	0.257
Length of NICU Stay	0.441	0.66
SNAPPE-II Score	-0.00569	0.998

Coefficient: Coefficients from the Linear Regression Model

P-value: Computed P-value Outcome: Neonatal Outcomes

APGAR1 Score: 1 minute APGAR score (scale from 1 to 10) **APGAR5 Score**: 5 minute APGAR score (scale from 1 to 10)

Length of NICU Stay: Length of stay at the Neonatal Intensive Care Unit, in days SNAPPE-II Score: Score for Neonatal Acute Physiology with Perinatal Extension-

II, score range: 0–20 (mild), 21–40 (moderate), 41 and higher (severe)

Table 3: Summary of key variables before and after new policy

PrePost	Pre	Post
Avg. Age	29.2	30.3
Avg. Gestational Age	39.7	39.6
Avg. Birth Wt.	3.46	3.42
Avg. APGAR1 Score	4.34	3.99
Avg. APGAR5 Score	7.4	7.14
Avg. NICU stay	7.52	7.96
Avg. SNAPPE-II Score	18.4	18.4

Avg. Age: Average age of the mother, years

Avg. Gestational Age: Average gestational age, weeks

Avg. Birth Wt.: Average birth weight in kilograms

Avg. APGAR1 Score: Average 1 minute APGAR score (scale from 1 to 10)

Avg. APGAR5 Score: Average 5 minute APGAR score (scale from 1 to 10)

Avg. NICU stay: Average length of stay at Neonatal Intensive Care Unit, in days

Avg. SNAPPE-II Score: Average Score for Neonatal Acute Physiology with Perinatal Extension-II, score range: 0–20 (mild), 21–40 (moderate), 41 and higher (severe)

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, O=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, 0=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, O=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
import numpy as np
Load the data
```

```
data =
    → pd.read_csv("meconium_nicu_dataset_preprocessed_short.csv
   # Replace NaN and infinite values with NaN.
   data = data.replace([np.inf, -np.inf], np.nan)
10
   # Open the output file
11
   with open('data_exploration.txt',
12
       # Data Size
13
       file.write("# Data Size\n")
14
       file.write(f"Number of rows: {data.shape[0]}\n")
15
       file write(f"Number of columns: {data.shape[1]}\n\n")
16
17
       # Summary Statistics
18
       file.write("# Summary Statistics\n")
19
       with pd.option_context('display.max_rows', None):
20
21
                file.write(f"{data.describe(include='all').round(2)}\n\n")
22
       # Categorical Variables
       file write("# Categorical Variables\n")
24
       cat_vars = data.select_dtypes(include=['object']).columns
25
       for cat in cat_vars:
26
            file.write(f"\n*** Variable: {cat} ***\n")
27
            val_count =
28
            \  \, \rightarrow \  \, data[cat].value\_counts(dropna=False).to\_string()
            file.write(f''\{val\_count\}\n\n'')
30
       # Average of 'ProlongedRupture' excluding NaN.
31
       if not data['ProlongedRupture'].isnull().values.any():
32
            file.write("# Average ProlongedRupture excluding
33
               NaN\n")
            file.write(f"Average ProlongedRupture:
               {data['ProlongedRupture'].mean():.2f}\n\n")
       # Average of 'SNAPPE_II_SCORE' excluding NaN.
36
       if not data['SNAPPE_II_SCORE'].isnull().values.any():
            file.write("# Average SNAPPE_II_SCORE excluding
38
            → NaN\n")
            file.write(f"Average SNAPPE_II_SCORE: \
39
```

```
{data['SNAPPE_II_SCORE'].mean():.2f}\n\n")
40
41
       # Missing Values
42
       file.write("# Missing Values\n")
43
       missing_values = data.isnull().sum()
44
       missing_values_pct = (missing_values /
45
            data.shape[0]).apply(lambda x: f'\{x:.2\%\}')
       missing_values = missing_values[missing_values
46
            0].astype(str)
       missing_values_pct = missing_values_pct[missing_values_pct
47
            != '0.00%']
       missing_values_df = pd.concat([missing_values,
48
            missing_values_pct], axis=1,
                                       keys=['Total Missing',
49
                                             Percent Missing'])
       file.write(f"{missing_values_df}
50
51
```

B.2 Code Description

The provided code performs data exploration on the given dataset. The main steps of the analysis can be summarized as follows:

- 1. Load the data: The code reads the dataset from a CSV file using the pandas library and stores it in a DataFrame.
- 2. Handle missing values: The code replaces any occurrences of infinite values or NaN with NaN.
- 3. Calculate data size: The code determines the number of rows and columns in the dataset and writes this information into the output file.
- 4. Calculate summary statistics: The code computes various summary statistics for the dataset using the 'describe' function of pandas DataFrame. It calculates basic statistics such as count, mean, standard deviation, minimum, quartiles, and maximum for numerical variables. For categorical variables, it provides the count of unique values.
- 5. Analyze categorical variables: The code identifies the categorical variables in the dataset and generates a frequency count of unique values for each categorical variable. This provides insights into the distribution and prevalence of different categories within each variable.
- 6. Calculate the average of 'ProlongedRupture': If the 'ProlongedRupture' variable does not contain any missing values, the code calculates the average value for this variable and writes it into the output file.

- 7. Calculate the average of 'SNAPPE_II_SCORE': If the 'SNAPPE_II_SCORE' variable does not contain any missing values, the code calculates the average value for this variable and writes it into the output file.
- 8. Handle missing values: The code identifies any missing values in the dataset and calculates the total number and percentage of missing values for each variable. It then writes this information into the output file.

The code writes the results of the data exploration analysis into the "data_exploration.txt" file. This file includes information about the data size, summary statistics, frequency counts for categorical variables, averages of specific variables (if applicable), and information on missing values in the dataset.

B.3 Code Output

$data_{exploration.txt}$

Data Size

Number of rows: 223 Number of columns: 34

Summary Statistics

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

		•	•							
count	223	223	223	223		223			223	
223		223		:	222	222		223		
223	223		223	223	223	223	3 223			
223	7		223			223		223		
223				223		223				223
223			223		223	223			223	
223		223		222						
unique	NaN	NaN	NaN	NaN		NaN			NaN	
2		NaN		Nal	N	NaN		3		
NaN	2		NaN	NaN	NaN	2	2 NaN	•		
NaN			NaN			NaN		3		

	NaN				NaN		NaN		NaN
	NaN			NaN		NaN	NaN	NaN	
	NaN		NaN		NaN				
top				NaN	NaN		NaN	NaN	
		AL		NaN		NaN	Na		
	NaN	M		NaN	NaN	NaN		CK NaN	
	NaN			NaN			NaN	RESP	
	NaN				NaN		NaN		NaN
	NaN			NaN		NaN	NaN	NaN	
	NaN		NaN						
fred	_			NaN			NaN	NaN	
	132		NaN				NaN	140	
	NaN	130		NaN	NaN	NaN	1	27 NaN	
	NaN			NaN			NaN	138	
	NaN				NaN		NaN		NaN
	NaN			NaN		NaN	NaN	NaN	
	NaN		NaN		NaN				
mear	1		29.72		1.42		0.03	0.12	
	NaN		0.34		0	.18	0.57	NaN	
	39.67	Nal	N		4.17	7.28		NaN 0.72	
	0.39		4	0.15			0.03	NaN	
	0.62				0.1		0.3		
	0.2		0.44			0.18		0.13	
	2.77		0.68				18.44		
std		0.5		1.43	0.92		0.16	0.32	
	NaN		0.48		0	.39		NaN	
	1.31	NaN		0.49	2.13	1.71		NaN 0.45	
	0.49			0.36			0.17	NaN	
	0.49				0.3		0.46		
	0.4		0.5			0.39		0.34	
	3.27		0.47	7	7.46		14.45		
min	1	0	16	1	0		0	0	
0	NaN		0			0	0	NaN	
	36	NaN	1	1.94	0	0	Na	N O	
	0			0			0	NaN	
	0				0		0		0
	0			0		0	0	0	
	0		2		0				
25%		0	26	1	1		0	0	
	NaN		0			0	0	NaN	

	39.05	NaN		16	2	7		NaN	0		
	0		0				0		NaN		
	0			0			0				0
	0		(0	0		0		1.	5	
	0	4		8.25							
50%		0	30	1	1			0		0	
	NaN		0		0		4	1	NaN		
	40.1	NaN	3.4	4	4	8		NaN	1		
	0		0				0		NaN		
	1			0			0				0
	0		(0	0		0		:	2	
	1	5		18		_ ()					
75%		1	34		2			0		0	
			1		0			1	NaN		
		NaN	3.8	1	6	8		NaN			
	1		0	W			0		NaN		
	1			0			1				0
	1		(0		0		;	3	
	1	8		24.5							
max		1	47	10	9			1		1	
			1		1			1	NaN		
		NaN	4.63	7	S)					
			1				1				
				1			1				1
		4	4	1	1		1		2	1	
		56))								
75% max	0 1 NaN 40.5 1 1	1 NaN	34 1 3.83 0 47 1 4.63	18 2 10 0 0 24.5 10 7 1	2 0 6 0		0 1 0	NaN 1 1	NaN 1 NaN	0	0

Categorical Variables

*** Variable: ModeDelivery ***

ModeDelivery VAGINAL 132 CS 91

*** Variable: Sepsis ***

Sepsis

NEG CULTURES 140 NO CULTURES 80 POS CULTURES 3

```
*** Variable: Gender ***
Gender
Μ
     130
F
      93
*** Variable: MeconiumConsistency ***
MeconiumConsistency
THICK
         127
THIN
          96
*** Variable: ReasonAdmission ***
ReasonAdmission
RESP
                     138
CHORIOAMNIONITIS
                      68
OTHER
                      17
# Missing Values
                 Total Missing Percent Missing
ProlongedRupture
                                           0.45%
Chorioamnionitis
                                           0.45%
SNAPPE_II_SCORE
                                           0.45%
```

C Data Analysis

C.1 Code

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

```
# IMPORT
import pandas as pd
import numpy as np
from scipy.stats import chi2_contingency
import statsmodels.formula.api as smf
import pickle
```

```
# LOAD DATA
   df =

→ pd.read_csv('meconium_nicu_dataset_preprocessed_short.csv')

11
   # DATASET PREPARATIONS
12
   # No dataset preparations are needed
13
14
   # DESCRIPTIVE STATISTICS
15
   ## Table 0: "Summary of key variables before and after new
    → policy"
   numeric_columns = ['AGE', 'GestationalAge',
                                                'BirthWeight',
       'APGAR1', 'APGAR5', 'LengthStay', 'SNAPPE_II_SCORE']
    df.groupby('PrePost')[numeric_columns].mean().reset_index()
   mean_df['PrePost'] = mean_df['PrePost'].map({0: 'Pre', 1:
   mean_df.set_index('PrePost', inplace=True)
   mean_df.to_pickle('table_0.pkl')
   # PREPROCESSING
23
   ## Creating dummy variables for categorical variables
24
   df = pd.get_dummies(df, columns=['ModeDelivery', 'Sepsis',
25
      'Gender', 'MeconiumConsistency', 'ReasonAdmission'])
26
   # ANALYSIS
27
   ## Table 1: "Association between change in new treatment
    → policy and changes in treatments"
   treatments = ['PPV', 'EndotrachealSuction',
29
        'MeconiumRecovered', 'CardiopulmonaryResuscitation',
                  'RespiratoryReasonAdmission',
30
                     'RespiratoryDistressSyndrome',
                     'TransientTachypnea',
                  'MeconiumAspirationSyndrome', 'OxygenTherapy',
                      'MechanicalVentilation', 'Surfactant',
                     'Pneumothorax',
                  'Breastfeeding']
   df1 = pd.DataFrame()
   for treatment in treatments:
```

```
contingency_table = pd.crosstab(df['PrePost'],
36

    df[treatment])
       chi2, p, _, _ = chi2_contingency(contingency_table)
37
       data_row = pd.DataFrame({'Treatment': [treatment],
        → 'Chi-square': [chi2], 'p-value': [p]})
       df1 = pd.concat([df1, data_row], ignore_index=True)
39
40
   df1.set_index('Treatment', inplace=True)
41
   df1.to_pickle('table_1.pkl')
42
43
   ## Table 2: "Linear regression analysis of
       change on neonatal outcomes"
   outcomes = ['APGAR1', 'APGAR5', 'LengthStay
45
       'SNAPPE_II_SCORE']
46
   df2 = pd.DataFrame()
47
   for outcome in outcomes:
48
       model = smf.ols(formula=f'{outcome} ~ PrePost', data=df)
49
       result = model.fit()
50
       data_row = pd.DataFrame({'Outcome': [outcome], 'Coeff':
51
            [result.params['PrePost']], 'p-value':
            [result.pvalues['PrePost']]})
       df2 = pd.concat([df2, data_row], ignore_index=True)
52
53
   df2.set_index('Outcome', inplace=True)
54
   df2.to_pickle('table_2.pkl')
56
   # SAVE ADDITIONAL RESULTS
57
   additional_results = {
58
    'Total number of observations': df.shape[0],
59
60
   with open('additional_results.pkl', 'wb') as f:
61
       pickle_dump(additional_results, f)
```

C.2 Code Description

The provided code performs data analysis on a dataset that compares Neonatal Resuscitation Program (NRP) therapies and clinical outcomes before and after the implementation of new guidelines in 2015. The dataset con-

tains information on various maternal and neonatal factors, treatments, and outcomes for 117 deliveries pre-guideline implementation and 106 deliveries post-guideline implementation.

The analysis is divided into several steps:

- 1. Loading the Dataset: The code reads the dataset from a CSV file, containing 44 columns.
- 2. Descriptive Statistics: The code calculates the mean values of key numeric variables (such as maternal age, gestational age, birth weight, etc.) for each group (pre- or post-guideline). These summary statistics are saved as a pickle file ('table_0.pkl').
- 3. Preprocessing of the Dataset: The code creates dummy variables for categorical variables using one-hot encoding.
- 4. Analysis of Treatments: The code performs a chi-squared test of independence to analyze the association between the change in treatment policy (pre- or post-guideline) and changes in various treatments. For each treatment, a contingency table is created and analyzed using chi-squared test. The results, including chi-square statistic and p-value, are saved as a pickle file ('table_1.pkl').
- 5. Analysis of Neonatal Outcomes: The code performs linear regression analysis to examine the impact of the policy change (pre- or post-guideline) on neonatal outcomes (e.g., APGAR1 score, APGAR5 score, length of stay, SNAPPE II score). For each outcome, a linear regression model is fitted, and the coefficient and p-value for the variable representing the policy change are extracted. The results are saved as a pickle file ('table_2.pkl').
- 6. Saving Additional Results: The code saves additional results, such as the total number of observations in the dataset, as a dictionary in a pickle file ('additional_results.pkl').

Overall, this code performs descriptive analysis, chi-squared test, and linear regression analysis to explore the impact of the NRP guideline change on treatments and neonatal outcomes. The results are stored in pickle files for further analysis and interpretation.

C.3 Code Output

table_0.pkl

AGE GestationalAge BirthWeight APGAR1 APGAR5 LengthStay SNAPPE_II_SCORE

PrePost
Pre 29.24 39.73 3.464 4.342 7.402 7.521

18.44
Post 30.25 39.59 3.419 3.991 7.142 7.962
18.43

$table_1.pkl$

	Chi-square	p-value
Treatment		
PPV	0.822	0.3646
EndotrachealSuction	50.52	1.182e-12
MeconiumRecovered	21.18	4.185e-06
CardiopulmonaryResuscitation	5.953	0.01469
RespiratoryReasonAdmission	1.162	0.2811
RespiratoryDistressSyndrome	0.8437	0.3584
TransientTachypnea	0.05744	0.8106
MeconiumAspirationSyndrome	0.9325	0.3342
OxygenTherapy	0	1
MechanicalVentilation	1.087	0.2972
Surfactant	0	1
Pneumothorax	1.176	0.2781
Breastfeeding	0.006255	0.937

$table_2.pkl$

Coeff p-value
Outcome
APGAR1 -0.3513 0.2202
APGAR5 -0.2602 0.2565
LengthStay 0.4409 0.6605
SNAPPE_II_SCORE -0.005693 0.9977

$additional_results.pkl$

'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]]]
8
   # PREPARATION FOR ALL TABLES
   def split_mapping(d: Mapping):
    abbrs_to_names = {abbr: name for abbr, (name, definition) in
11

    d.items() if name is not None}

    names_to_definitions = {name or abbr: definition for abbr,
    → (name, definition) in d items() if definition is not
       None}
    return abbrs_to_names, names_to_definitions
13
14
   shared_mapping: Mapping = {
15
    'AGE': ('Avg. Age', 'Average age of the mother, years'),
16
    'Gestational Age': ('Avg. Gestational Age', 'Average
17

→ gestational age, weeks'),
    'BirthWeight': ('Avg. Birth Wt.', 'Average birth weight in
    'APGAR1': ('Avg. APGAR1 Score', 'Average 1 minute APGAR score
19
    \rightarrow (scale from 1 to 10)'),
    'APGAR5': ('Avg. APGAR5 Score', 'Average 5 minute APGAR score
    'LengthStay': ('Avg. NICU stay', 'Average length of stay at
    → Neonatal Intensive Care Unit, in days'),
    'SNAPPE_II_SCORE': ('Avg. SNAPPE-II Score', 'Average Score
        for Neonatal Acute Physiology with Perinatal
        Extension-II, score range: 0{20 (mild), 21{40 (moderate),
        41 and higher (severe)'),
23
24
```

```
# TABLE 0
25
   df0 = pd.read_pickle('table_0.pkl')
26
27
   # Transpose data
   df0 = df0.T
29
30
   # Apply shared mapping
31
   mapping = {k: v for k, v in shared_mapping.items() if

→ df0.columns or k in df0.index}
   abbrs_to_names, legend = split_mapping(mapping)
33
   df0 = df0.rename(columns=abbrs_to_names, index=abbrs_to_names)
35
   # Save as latex
36
   to_latex_with_note(
37
    df0, 'table_0.tex',
38
    caption='Summary of key variables before and after new
39
     → policy',
    label='table:SummaryVariables
40
    legend=legend)
41
42
43
   # TABLE 1
44
   df1 = pd.read_pickle('table_1.pkl')
45
46
   # Renaming the labels with scientifically-suitable names
47
   mapping1: Mapping = {
48
    'Chi-square': ('Chi-square', 'Chi-square Test Statistic'),
49
    'p-value': ('P-value', 'Computed P-value'),
50
    'Treatment': ('Treatment', 'Types of Neonatal Treatments'),
51
    'PPV': ('PPV (Positive Pressure Ventilation)', 'Whether
52
     \rightarrow positive pressure ventilation was performed, 1:Yes,
     \rightarrow 0:No'),
     EndotrachealSuction': ('Endotracheal Suction', 'Whether
        endotracheal suctioning was performed, 1:Yes, 0:No'),
    'MeconiumRecovered': ('Meconium Recovered', 'Whether Meconium
        was recovered, 1:Yes, 0:No'),
    'CardiopulmonaryResuscitation': ('Cardiopulmonary
        Resuscitation', 'Whether cardiopulmonary resuscitation
        was performed, 1:Yes, 0:No'),
```

```
'RespiratoryReasonAdmission': ('Reason for Admission -
56
     → Respiratory ', 'Admission due to respiratory reason,
       1:Yes, 0:No'),
    'RespiratoryDistressSyndrome': ('Respiratory Distress
57
     → Syndrome', 'Presence of respiratory distress syndrome,
     \rightarrow 1:Yes, 0:No'),
    'TransientTachypnea': ('Transient Tachypnea', 'Presence of
58

    transient tachypnea, 1:Yes, 0:No'),
    'MeconiumAspirationSyndrome': ('Meconium Aspiration
59

→ Syndrome', 'Presence of meconium aspiration syndrome,
     \rightarrow 1:Yes, 0:No'),
    'OxygenTherapy': ('Oxygen Therapy', 'Whether oxygen therapy

→ was given, 1:Yes, 0:No'),
    'Mechanical Ventilation': ('Mechanical Ventilation',
61
        'Mechanical Ventilation performed, 1:Yes, 0:No')
   }
62
63
   abbrs_to_names1, legend1 = split_mapping(mapping1)
   df1 = df1.rename(columns=abbrs_to_names1,

→ index=abbrs_to_names1)
66
   # Formatting P-value
67
   df1["P-value"] = df1["P-value"] .map(format_p_value)
68
69
   # Save as latex
70
   to_latex_with_note(
71
    df1, 'table_1.tex',
72
    caption='Association between change in new treatment policy
     → and changes in treatments',
    label='table:TreatmentPolicyChange',
74
    legend=legend1
75
76
77
     TABLE 2
   df2 = pd.read_pickle('table_2.pkl')
80
   # Renaming abbreviated labels
   mapping2: Mapping = {
    'Coeff': ('Coefficient', 'Coefficients from the Linear
     → Regression Model'),
```

```
'p-value': ('P-value', 'Computed P-value'),
     'Outcome': ('Outcome', 'Neonatal Outcomes'),
85
     'APGAR1': ('APGAR1 Score', '1 minute APGAR score (scale from
86
     \rightarrow 1 to 10)'),
     'APGAR5': ('APGAR5 Score', '5 minute APGAR score (scale from
     \rightarrow 1 to 10)'),
     'LengthStay': ('Length of NICU Stay', 'Length of stay at the
     → Neonatal Intensive Care Unit, in days'),
     'SNAPPE_II_SCORE': ('SNAPPE-II Score', 'Score for Neonatal
89
     → Acute Physiology with Perinatal Extension-II, score range:
        0{20 (mild), 21{40 (moderate), 41 and higher (severe)'),
90
91
    abbrs_to_names2, legend2 = split_mapping(mapping2)
92
    df2 = df2.rename(columns=abbrs_to_names2,
       index=abbrs_to_names2)
94
    # Formatting P-value
95
    df2["P-value"] = df2["P-value"].map(format_p_value)
    # Save as latex
98
    to_latex_with_note(
99
     df2, 'table_2.tex',
100
     caption='Linear regression analysis of impact of policy
101

→ change on neonatal outcomes',

     label='table:PolicyImpactOutcomes',
102
     legend=legend2)
104
105
         Code Output
    table\_0.tex
    \begin{table}[h]
    \caption{Summary of key variables before and after new policy}
    \label{table:SummaryVariables}
    \begin{threeparttable}
    \renewcommand{\TPTminimum}{\linewidth}
    \makebox[\linewidth]{%
```

84

```
\begin{tabular}{lrr}
\toprule
PrePost & Pre & Post \\
\midrule
\textbf{Avg. Age} & 29.2 & 30.3 \\
\textbf{Avg. Gestational Age} & 39.7 & 39.6 \\
\textbf{Avg. Birth Wt.} & 3.46 & 3.42 \\
\textbf{Avg. APGAR1 Score} & 4.34 & 3.99 \\
\textbf{Avg. APGAR5 Score} & 7.4 & 7.14 \\
\textbf{Avg. NICU stay} & 7.52 & 7.96 \\
\textbf{Avg. SNAPPE-II Score} & 18.4 & 18.4
\bottomrule
\end{tabular}}
\begin{tablenotes}
\footnotesize
\item \textbf{Avg. Age}: Average age of the mother, years
\item \textbf{Avg. Gestational Age}: Average gestational age, weeks
\item \textbf{Avg. Birth Wt.}: Average birth weight in kilograms
\item \textbf{Avg. APGAR1 Score}: Average 1 minute APGAR score (scale from 1 to
\item \textbf{Avg. APGAR5 Score}: Average 5 minute APGAR score (scale from 1 to
\item \textbf{Avg. NICU stay}: Average length of stay at Neonatal Intensive Care
   Unit, in days
\item \textbf{Avg. SNAPPE-II Score}: Average Score for Neonatal Acute Physiology
    with Perinatal Extension-II, score range: 0{20 (mild), 21{40 (moderate), 41 and
    higher (severe)
\end{tablenotes}
\end{threeparttable}
\end{table}
table_1.tex
\begin{table}[h]
caption{Association between change in new treatment policy and changes in
    treatments}
\label{table:TreatmentPolicyChange}
```

\begin{threeparttable}

\renewcommand{\TPTminimum}{\linewidth}

```
\makebox[\linewidth]{%
\begin{tabular}{lrl}
\toprule
 & Chi-square & P-value \\
Treatment & & \\
\midrule
\textbf{PPV (Positive Pressure Ventilation)} & 0.822 & 0.365 \\
\textbf{Endotracheal Suction} & 50.5 & $<$1e-06 \\
\textbf{Meconium Recovered} & 21.2 & 4.19e-06 \\
\textbf{Cardiopulmonary Resuscitation} & 5.95 & 0.0147 \\
\textbf{Reason for Admission - Respiratory } & 1.16 & 0.281 \\
\textbf{Respiratory Distress Syndrome} & 0.844 & 0.358 \\
\textbf{Transient Tachypnea} & 0.0574 & 0.811 \\
\textbf{Meconium Aspiration Syndrome} & 0.932 & 0.334 \\
\textbf{Oxygen Therapy} & 0 & 1 \\
\textbf{Mechanical Ventilation} & 1.09 & 0.297 \\
\textbf{Surfactant} & 0 & 1 \\
\textbf{Pneumothorax} & 1.18 & 0.278 \\
\textbf{Breastfeeding} & 0.00626 & 0.937 \\
\bottomrule
\end{tabular}}
\begin{tablenotes}
\footnotesize
\item \textbf{Chi-square}: Chi-square Test Statistic
\item \textbf{P-value}: Computed P-value
\item \textbf{Treatment}: Types of Neonatal Treatments
\item \textbf{PPV (Positive Pressure Ventilation)}: Whether positive pressure
    ventilation was performed, 1:Yes, 0:No
\item \textbf{Endotracheal Suction}: Whether endotracheal suctioning was
    performed, 1:Yes, 0:No
\item \textbf{Meconium Recovered}: Whether Meconium was recovered, 1:Yes, 0:No
\item \textbf{Cardiopulmonary Resuscitation}: Whether cardiopulmonary
   resuscitation was performed, 1:Yes, 0:No
\item \textbf{Reason for Admission - Respiratory }: Admission due to respiratory
    reason, 1:Yes, 0:No
\item \textbf{Respiratory Distress Syndrome}: Presence of respiratory distress
    syndrome, 1:Yes, 0:No
\item \textbf{Transient Tachypnea}: Presence of transient tachypnea, 1:Yes, 0:No
\item \textbf{Meconium Aspiration Syndrome}: Presence of meconium aspiration
```

syndrome, 1:Yes, 0:No

```
\item \textbf{Oxygen Therapy}: Whether oxygen therapy was given, 1:Yes, 0:No
\item \textbf{Mechanical Ventilation}: Mechanical Ventilation performed, 1:Yes,
    0:No
\end{tablenotes}
\end{threeparttable}
\end{table}
table_2.tex
\begin{table}[h]
\caption{Linear regression analysis of impact of policy change on neonatal
    outcomes}
\label{table:PolicyImpactOutcomes}
\begin{threeparttable}
\renewcommand{\TPTminimum}{\linewidth}
\makebox[\linewidth]{%
\begin{tabular}{lrl}
\toprule
 & Coefficient & P-value
Outcome & & \\
\midrule
\textbf{APGAR1 Score} & -0.351 & 0.22 \\
\textbf{APGAR5 Score} & -0.26 & 0.257 \\
\textbf{Length of NICU Stay} & 0.441 & 0.66 \\
\textbf{SNAPPE-II Score} & -0.00569 & 0.998 \\
\bottomrule
\end{tabular}}
\begin{tablenotes}
\footnotesize
\item \textbf{Coefficient}: Coefficients from the Linear Regression Model
\item \textbf{P-value}: Computed P-value
\item \textbf{Outcome}: Neonatal Outcomes
\item \textbf{APGAR1 Score}: 1 minute APGAR score (scale from 1 to 10)
\item \textbf{APGAR5 Score}: 5 minute APGAR score (scale from 1 to 10)
\item \textbf{Length of NICU Stay}: Length of stay at the Neonatal Intensive
    Care Unit, in days
\item \textbf{SNAPPE-II Score}: Score for Neonatal Acute Physiology with
    Perinatal Extension-II, score range: 0{20 (mild), 21{40 (moderate), 41 and higher
    (severe)
```

\end{tablenotes}
\end{threeparttable}
\end{table}

References

- [1] E. Boyle, S. Johnson, B. Manktelow, S. Seaton, E. Draper, Lucy K Smith, J. Dorling, N. Marlow, S. Petrou, and D. Field. Neonatal outcomes and delivery of care for infants born late preterm or moderately preterm: a prospective population-based study. *Archives of Disease in Childhood. Fetal and Neonatal Edition*, 100:F479 F485, 2015.
- [2] D. Chawla, D. Chirla, S. Dalwai, A. Deorari, A. Ganatra, A. Gandhi, N. Kabra, Praveen Kumar, P. Mittal, B. Parekh, M. J. Sankar, T. Singhal, S. Sivanandan, P. Tank, Federation of Obstetric, Gynaecological Societies of India, National Neonatology Forum of India, and Indian Academy of Pediatrics. Perinatal-neonatal management of covid-19 infection guidelines of the federation of obstetric and gynaecological societies of india (fogsi), national neonatology forum of india (nnf), and indian academy of pediatrics (iap). *Indian Pediatrics*, 57:536 548, 2020.
- [3] B. Stoll, N. Hansen, E. Bell, S. Shankaran, A. Laptook, M. Walsh, E. Hale, N. Newman, K. Schibler, W. Carlo, K. Kennedy, B. Poindexter, N. Finer, R. Ehrenkranz, S. Duara, P. Snchez, T. O'Shea, R. Goldberg, K. V. van Meurs, R. Faix, D. Phelps, I. Frantz, K. Watterberg, S. Saha, A. Das, and R. Higgins. Neonatal outcomes of extremely preterm infants from the nichd neonatal research network. *Pediatrics*, 126:443 456, 2010.
- [4] M. Wyckoff, K. Aziz, M. Escobedo, V. Kapadia, J. Kattwinkel, J. Perlman, W. Simon, G. Weiner, and J. Zaichkin. Part 13: Neonatal resuscitation: 2015 american heart association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*, 132 18 Suppl 2:S543–60, 2015.
- [5] H. Halliday and D. Sweet. Endotracheal intubation at birth for preventing morbidity and mortality in vigorous, meconium-stained infants born at term. The Cochrane database of systematic reviews, 2:CD000500, 2001.

- [6] K. Hishikawa, H. Fujinaga, T. Fujiwara, Keiji Goishi, M. Kaneshige, H. Sago, and Yushi Ito. Respiratory stabilization after delivery in term infants after the update of the japan resuscitation council guidelines in 2010. Neonatology, 110:1 – 7, 2016.
- [7] E. O. Boundy, R. Dastjerdi, D. Spiegelman, W. Fawzi, S. Missmer, E. Lieberman, S. Kajeepeta, S. Wall, and G. Chan. Kangaroo mother care and neonatal outcomes: A meta-analysis. *Pediatrics*, 137, 2016.
- [8] C. Salvatore, Jin-Young Han, Karen P. Acker, P. Tiwari, Jenny C Jin, M. Brandler, C. Cangemi, L. Gordon, A. Parow, Jennifer I Dipace, and P. Delamora. Neonatal management and outcomes during the covid-19 pandemic: an observation cohort study. The Lancet. Child & Adolescent Health, 4:721 727, 2020.
- [9] S. Daga, K. Dave, V. Mehta, and V. Pai. Tracheal suction in meconium stained infants: a randomized controlled study. *Journal of tropical* pediatrics, 40 4:198–200, 1994.
- [10] E. Gulczyska and J. Gadzinowski. Practical aspects of therapeutic hypothermia in neonates with hypoxic ischemic encephalopathy–questions and answers. part i. providing newborn care before and during transfer to the reference center. *Developmental period medicine*, 19 3 Pt 1:247–53, 2015.
- [11] H. Al-shehri. The use of alcohol versus dry care for the umbilical cord in newborns: A systematic review and meta-analysis of randomized and non-randomized studies. *Cureus*, 11, 2019.
- [12] Peter A. Johnson and G. Schmlzer. Heart rate assessment during neonatal resuscitation. *Healthcare*, 8, 2020.
- [13] K. Goeral, Gregor Kasprian, L. Schmidt, Francesco Cardona, Angelika Berger, and K. Klebermass-Schrehof. Po-0394is acute kidney injury related to worse outcomes in newborns treated with hypothermia? Archives of Disease in Childhood, 99:A374 – A375, 2014.
- [14] Study, MohdYunus, V. Agarwal, P. Tomer, Priyanka Gupta, and A. Upadhyay. Epidemiology, clinical spectrum and outcomes of fungal sepsis in neonates in neonatal intensive care unit: A prospective observational study. 2018.

- [15] L. Mileder, Michael Bereiter, and T. Wegscheider. Telesimulation as a modality for neonatal resuscitation training. *Medical Education Online*, 26, 2021.
- [16] M. Lindhard, Signe Thim, H. Laursen, A. Schram, C. Paltved, and T. Henriksen. Simulation-based neonatal resuscitation team training: A systematic review. *Pediatrics*, 147, 2021.
- [17] Rayees Rahman, A. Kodesh, S. Levine, S. Sandin, A. Reichenberg, and A. Schlessinger. Identification of newborns at risk for autism using electronic medical records and machine learning. *European Psychiatry*: the journal of the Association of European Psychiatrists, 63, 2019.
- [18] A. Barra, P. Contucci, Rickard Sandell, and C. Vernia. An analysis of a large dataset on immigrant integration in spain. the statistical mechanics perspective on social action. *Scientific Reports*, 4, 2013.
- [19] Shrishail Gidaganti, M. Faridi, M. Narang, and P. Batra. Effect of gastric lavage on meconium aspiration syndrome and feed intolerance in vigorous infants born with meconium stained amniotic fluid a randomized control trial. *Indian Pediatrics*, 55:206–210, 2018.
- [20] D. Trevisanuto, Laura Moschino, N. Doglioni, C. Roehr, M. Gervasi, and E. Baraldi. Neonatal resuscitation where the mother has a suspected or confirmed novel coronavirus (sars-cov-2) infection: Suggestion for a pragmatic action plan. Neonatology, pages 1 8, 2020.
- [21] D. Jaye and KenB. Waites. Clinical applications of c-reactive protein in pediatrics. *The Pediatric infectious disease journal*, 16 8:735–46; quiz 746–7, 1997.
- [22] D. Flannery, S. Gouma, Miren B Dhudasia, S. Mukhopadhyay, M. Pfeifer, E. Woodford, Jourdan E. Triebwasser, J. Gerber, Jeffrey S. Morris, M. Weirick, C. McAllister, M. Bolton, C. P. Arevalo, E. M. Anderson, E. Goodwin, S. Hensley, and K. Puopolo. Assessment of maternal and neonatal cord blood sars-cov-2 antibodies and placental transfer ratios. JAMA pediatrics, 2021.
- [23] Tracy A. Wolff, E. Shelton, C. Sessions, and Therese L Miller. Screening for syphilis infection in pregnant women: Evidence for the u.s. preventive services task force reaffirmation recommendation statement. *Annals of Internal Medicine*, 150:710–716, 2009.

- [24] F. Jansen, R. Prins, Astrid Etman, H. P. van der Ploeg, S. D. de Vries, F. V. van Lenthe, and F. Pierik. Physical activity in non-frail and frail older adults. *PLoS ONE*, 10, 2015.
- [25] M. Menai, V. V. van Hees, A. Elbaz, M. Kivimaki, A. SinghManoux, and S. Sabia. Accelerometer assessed moderate-to-vigorous physical activity and successful ageing: results from the whitehall ii study. Scientific Reports, 7, 2017.
- [26] K. Westerterp. Impacts of vigorous and non-vigorous activity on daily energy expenditure. *Proceedings of the Nutrition Society*, 62:645 650, 2003.