

# Factors associated with successful extubation following the use of systemic dexamethasone in ventilator dependent extremely preterm infants with bronchopulmonary dysplasia

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June 21, 2021

## Abstract

**Objectives** The aim of our study was to identify, in mechanically ventilated neonates <30 weeks GA with clinical evidence of bronchopulmonary dysplasia (BPD), factors likely to be predictive of a first course of systemic dexamethasone leading to extubation within 14 days and remaining extubated for at least 7 days. **Methods** We studied a retrospective cohort of neonates (23+0-29+6 weeks GA), with evidence of BPD, prescribed their first course of systemic dexamethasone to aid in extubation from mechanical ventilation. The data collected only pertained to the first course of dexamethasone for any given neonate, with the primary outcome of interest of successful extubation within 14 days (i.e., extubated within 14 days of starting dexamethasone and remaining extubated for at least seven days). Binary logistic regression was employed. **Results** A total of 287 neonates were included. Each additional week of GA at birth led to a 1.53 increase in the odds of successful extubation (95% CI 1.122-2.096,  $p<0.01$ ). Higher average fraction of inspired oxygen (FiO<sub>2</sub>) requirements in the preceding 24 hours resulted in a 0.94 decrease in the odds of successful extubation ( $p<0.05$ ) and higher mean airway pressure (MAP) resulted in 0.76 decrease in odds of successful extubation ( $p<0.01$ ). **Conclusions** Mechanically ventilated neonates born at <30 week GA, with evidence of BPD requiring dexamethasone to facilitate extubation, had a lower likelihood of successful extubation by day 14 if at the time of commencing steroids they were less mature at birth, had higher MAPs and higher oxygen requirements.

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## Methods

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## Results

A total of 287 neonates were included. Each additional week of GA at birth led to a 1.53 increase in the odds of successful extubation (95% CI 1.122-2.096,  $p < 0.01$ ). Higher average fraction of inspired oxygen (FiO<sub>2</sub>) requirements in the preceding 24 hours resulted in a 0.94 decrease in the odds of successful extubation ( $p < 0.05$ ) and higher mean airway pressure (MAP) resulted in 0.76 decrease in odds of successful extubation ( $p < 0.01$ ).

## Conclusions

Mechanically ventilated neonates born at <30 week GA, with evidence of BPD requiring dexamethasone to facilitate extubation, had a lower likelihood of successful extubation by day 14 if at the time of commencing steroids they were less mature at birth, had higher MAPs and higher oxygen requirements.

## INTRODUCTION

Most extremely preterm neonates require mechanical ventilation.<sup>1</sup> Once they are intubated, the aim is to extubate as soon as possible to minimise time spent mechanically ventilated. The desired outcome is to reduce the risk of the development of chronic lung disease, aka bronchopulmonary dysplasia (BPD), and associated adverse outcomes.<sup>2-4</sup>

The chronic lung disease, which often requires further prolonged periods of intubation, involves inflammatory parenchymal change with incremental increases in inspired oxygen, inflation pressures and tidal volume to achieve adequate gas exchange.<sup>5</sup> BPD is still common; occurring in 80% of neonates less than 25 weeks gestational age (GA).<sup>6</sup> The risk is higher in very low birthweight neonates who remain intubated after 1-2 weeks of age.<sup>3</sup> Systemic dexamethasone facilitates weaning of invasive ventilatory support by suppressing inflammation, improving lung compliance, and decreasing airway resistance.<sup>5-8</sup> There are well documented complications of systemic steroids: gastric perforation and bleeding, hypertension, hyperglycaemia, poor growth and worse neurodevelopmental outcome.<sup>8-11</sup> Therefore, steroids are often reserved for neonates who are difficult to extubate from mechanical ventilation, who exhibit clinical evidence of BPD and are greater than 7 days of age; and where the risk of BPD is >50%.<sup>12</sup> Clinicians should also aim to give with the lowest cumulative dose of steroids.<sup>9,13,14</sup>

Responses to the initial dexamethasone courses are variable, at times resulting in dexamethasone treatment that does not facilitate extubation. There may be factors present at the time of considering treating the

neonate with steroids that are associated with a lesser or greater chance of successful extubation. If factors are identified that are associated with a reduction in successful extubation, it may well be worth electing to wait until circumstances are more favourable. Given the paucity of research investigating these potential factors, the aim of our study was to identify, in mechanically ventilated neonates less than 30 weeks GA with clinical evidence of BPD, predictors that are associated with a first course of systemic dexamethasone leading to extubation within 14 days and remaining extubated for at least 7 days.

## METHODS

### Study participants

Our unit is a metropolitan tertiary neonatal unit. All neonates prescribed their first course of systemic dexamethasone to aid in extubation from mechanical ventilation with evidence of BPD, who were born at <30 weeks GA between January 2007 to December 2017 and admitted to the GSNU, were eligible to be included in the retrospective cohort study. The timing and dose of dexamethasone was determined by the neonate's treating neonatologist. The treatment plan was chosen from a range of dexamethasone dosing regimens. Neonates who received dexamethasone were identified using the NeoDATA database.

Inclusion criteria:

- born at 23<sup>+0</sup>-29<sup>+6</sup> weeks GA,
- admitted to the unit,
- mechanically ventilated,
- received systemic dexamethasone,
- had or were at high risk of developing BPD

Exclusion criteria

- congenital airway or lung lesion,
- lung pathology other than BPD,
- GA <23 or [?]30 weeks,
- steroids given for stridor and/or subglottic oedema.

This study was considered exempt from full ethical review by the Royal Brisbane and Women's Hospital Human Research Ethics Committee with no requirement for parental informed consent given the retrospective, de-identified data collected.

### Measurements

The data collected only pertained to the first course of dexamethasone for any given neonate, including demographic and historical data: birth-weight (BW), gestational age (GA), sex, antenatal corticosteroids, surfactant (number of doses), mode of delivery, maternal infection, oligohydramnios, patent ductus arteriosus (PDA), anaemia and previous episodes of sepsis, and air leaks.

Data were also collected on the neonate's circumstances at the time of commencing systemic steroids: date commenced and starting dose of dexamethasone (mg/kg/day), ventilation mode (conventional vs high frequency ventilation (HFOV)), average fraction of inspired oxygen (FiO<sub>2</sub>) in preceding 24 hours, days on mechanical ventilation, previous extubation attempts, corrected GA, postnatal age, chest x-ray appearance, weight, parenteral nutrition (PN) use, whether receiving enteral feeds, type of enteral feed, total fluid volumes (mL/kg/day), partial pressure of carbon dioxide on blood gas (pCO<sub>2</sub>), mean airway pressure (MAP), oxygen saturations (SpO<sub>2</sub>) over preceding 24 hours, date extubated, and whether antibiotics were being used.

Data collected after dexamethasone commencement included the primary outcome of interest: was neonate *successfully extubated* within 14 days? *Successfully extubated* was defined as extubated within 14 days of starting dexamethasone and remaining extubated for at least seven days.

The last chest x-ray prior to the commencement of dexamethasone was graded by an independent neonatologist using the system of Kim<sup>15</sup> based on interstitial lung changes associated with BPD: grade 1 – no abnormality; grade 2 – granular infiltration; grade 3 – diffuse streaky interstitial infiltration; grade 4 – diffuse course reticular infiltration.

### Data analysis

As the study was retrospective (the sample size was fixed *a priori*) and exploratory, the 10 cases per covariate approach to sample size calculation was used to establish, prospectively, that our sample size of 300 was likely to be sufficient.<sup>16</sup> Descriptive statistics included medians and inter-quartile ranges for continuous variables (including time-to-event variables) and counts and percentages for categorical variables. Initial summary statistics of the whole cohort and comparison tests between two groups, those successfully extubated by 14 days after starting dexamethasone and those not successfully extubated in that time, were done using GraphPad Prism 8 (GraphPad Software LLC, San Diego, CA, USA).

As the primary outcome in the present study is a binary variable, binary logistic regression was employed. Univariate and multivariable binary logistic regression models were fit to the data to produce unadjusted and adjusted odds ratios, respectively, along with their corresponding 95% confidence intervals. The multivariable model included all potentially important predictors (independent risk factors and confounders) including clinically important variables and those with a  $p < 0.2$  in the univariate analysis. All modelling was conducted using the R statistical package (v4.0.2; The R Project for Statistical Computing, [www.r-project.org/](http://www.r-project.org/)) and a p-value less than 0.05 was used to represent statistical significance throughout all inferential analyses.

### RESULTS

A total of 287 neonates were included (see Figure 1); see Table 1 for their demographics and clinical characteristics.

Figure 1. Recruitment flow chart for infants into the retrospective study born between 1<sup>st</sup> January 2007 to 31<sup>st</sup> December 2017 at GSNU

**Table 1.** Description of the whole sample (n=287) before or at the time of starting dexamethasone.

Variable		Summary statistics
GA (weeks) – median (IQR)		25.3 (24.4-26.3)
BW (grams) – median (IQR)		720 (624-839)
Male – N (%)		181 (63)
Inborn - N (%)		233 (81)
Multiples - N (%)		94 (33)
Oligohydramnios - N (%)		20 (7)
Chorioamnionitis - N (%)		82 (29)
Antenatal steroids - N (%)	nil	12 (4)
	<24 hours	90 (31)
	completed	176 (62)
	> 7days	9 (3)
No. of doses of postnatal surfactant - N (%)	0	3 (1)
	1	48 (17)
	2	227 (79)
	3	8 (2.7)
	4	1 (0.3)
No. of prior failed extubation attempts - N (%)	0	196 (69)
	1	70 (24)
	2	20 (6.7)
	3	1 (0.3)

Variable	Summary st	
Days ventilated prior to dexamethasone - median (IQR)	12 (10-29)	
Age at starting dexamethasone (days) - median (IQR)	19 (15-27)	
GA at dexamethasone (weeks) - median (IQR)	28.3 (27-29.8)	
Weight at starting dexamethasone (grams)- median (IQR)	990 (819-1180)	
Starting dose of dexamethasone (mg/kg/day)- median (IQR)	0.17 (0.15-0.48)	
IVABx prior to/at dexamethasone commencement (%)	223 (78)	
Total fluid intake (mL/kg/day)- median (IQR)	172 (157-180)	
PN- N (%)	120 (42)	
Enteral feeding - N (%)	NBM	8 (2.8)
	breastmilk only	255 (89)
	formula	20 (6.9)
	mixed	4 (1.3)
	echo/open	140 (49)
PDA status- N (%)	echo/closed	61 (21)
	presumed open	33 (11)
	presumed closed	53 (19)
	HFOV	74 (26)
	conventional	213 (74)
MAP (cm H <sub>2</sub> O) - median (IQR)	12 (10-13)	
Average FiO <sub>2</sub> 24 hours prior to dexamethasone - median (IQR)	0.36 (0.31-0.41)	
Average SpO <sub>2</sub> in 24 hr prior to dexamethasone - median (IQR)	90 (89-91)	
Last pH before starting dexamethasone - median (IQR)	7.29 (7.24-7.33)	
<b>Variable</b>	<b>Summary st</b>	
Last pCO <sub>2</sub> before starting dexamethasone - median (IQR)	57 (51-62)	
Last Hb before starting dexamethasone (g/L) - median (IQR)	108 (94-123)	
Previous sepsis- N (%)	nil	260 (91)
	before dexamethasone	20 (7)
	within 5 days of starting dexamethasone	7 (2)
	nil	221 (77)
Previous airleaks - N (%)	pneumothorax	31 (10.8)
	PIE	22 (7.6)
	both	13 (4.4)
	nil	221 (77)
CXR findings - N (%)	grade 1	4 (1.4)
	grade 2	169 (59)
	grade 3	98 (34)
	grade 4	16 (5.6)

Gestational Age (GA), birthweight (BW), Intravenous antibiotics (IVABx), total parental nutrition (TPN), Patent Ductus Arteriosus (PDA), High Frequency Oscillation ventilation (HFOV), Mean Airway Pressure (MAP), inspired oxygen (FiO<sub>2</sub>), oxygen saturations (SpO<sub>2</sub>), partial pressure of carbon dioxide on blood gas (pCO<sub>2</sub>), Haemoglobin (Hb), Pulmonary interstitial emphysema (PIE), chest xray (CXR)

Table 2 shows the comparisons between the two groups; *successfully extubated* (N=175) and *not successfully extubated* (N = 112) within 14 days of commencing dexamethasone. Compared with those that were not successfully extubated, those who were successfully extubated were more mature at birth or had higher birthweights. They were also heavier at the time of starting dexamethasone and more mature (corrected GA), and older (postnatal age in days). Successfully extubated babies were more likely off PN. These infants also had less severe BPD on their chest x-rays.

Those not successfully extubated by 14 days after starting dexamethasone were more likely to have had: a

recent echocardiogram that showed a PDA, higher MAPs and FiO<sub>2</sub> requirements and ventilated using HFOV at the time of starting dexamethasone.

**Table 2.** Univariate analysis between the two groups: *successfully extubated* within 14 days of commencing dexamethasone and *not successfully extubated* .

Variable	Successfully extubated by day 14	NOT successfully extubated
	N = 175	N= 112
GA – median (IQR)	25.9 (24.9-26.9)	24.7 (24.1-25.6)
BW – median (IQR)	762 (651-882)	674 (599-752)
Male – N (%)	109 (62)	72 (64)
Inborn- N (%)	139 (79)	94 (84)
Oligohydramnios - N (%)	12 (7)	8 (7)
Chorioamnionitis- N (%)	41 (23)	41 (37)
Antenatal steroids- N (%)		
None/ <24hrs	65 (37)	37 (33)
Completed course / > 7 days	110 (63)	75 (67)
Postnatal Surfactant- N (%)	172 (98)	112 (100)
Failed extubation attempts before dexamethasone (%)		
0	107 (61)	89 (79)
1	52 (30)	18 (16)
2 or more	16 (9)	5 (4)
Days ventilated prior to dexamethasone - median (IQR)	16 (13-22)	15 (12-19)
Age at starting dexamethasone (days) - median (IQR)	22 (16-29)	17 (14-23)
GA at dexamethasone (weeks) - median (IQR)	28.9 (27.9-30.7)	27.3 (26.4-28.5)
Weight at starting dexamethasone (grams) - median (IQR)	1075 (910-1262)	863 (744-1050)
Starting dose of dexamethasone (mg/kg/day) - median (IQR)	0.29 (0.15-0.49)	0.16 (0.15-0.47)
IVABx prior to/at dexamethasone - N (%)	132 (75)	91 (81)
Total fluid intake (mL/kg/day)- median (IQR)	173 (156-180)	171 (157 -180)
PN- N (%)	69 (39)	51 (46)
Enteral feeding - N (%)	173 (99)	106 (95)
PDA status at start of dexamethasone - N (%)		
echo/open	73 (42)	67 (60)
echo/closed	34 (19)	27 (21)
presumed open	26 (15)	7 (6)
presumed closed	42 (24)	11 (10)
Ventilation mode at start dexamethasone - N (%)		
Conventional	143 (82)	70 (63)
HFOV	32 (18)	42 (38)
MAP (cm H <sub>2</sub> O)- median (IQR)	11 (10-12)	13 (11-14)
Average FiO <sub>2</sub> 24 hr prior to dexamethasone - median (IQR)	0.35 (0.30-0.39)	0.40 (0.33-0.48)
Average SpO <sub>2</sub> 24 hr prior to dexamethasone - median (IQR)	90 (89-92)	90 (89-91)
Last pH before starting dexamethasone - median (IQR)	7.30 (7.25-7.33)	7.28 (7.23-7.34)
Last pCO <sub>2</sub> before starting dexamethasone - median (IQR)	57.9 (52.0-62.1)	56.0 (51.0-62.9)
Last Hb before starting dexamethasone (g/L)- median (IQR)	108 (94-124)	106 (94-122)
Previous sepsis- N (%)	16 (9)	11 (10)
Previous airleaks- N (%)		
nil	139 (79)	82 (73)
Pneumothorax	18 (10)	13 (12)
PIE	8 (5)	14 (13)
Both	10 (6)	3 (3)
CXR appearance- N (%)		

Variable	Successfully extubated by day 14	NOT successful
Grade 1 / 2	122 (70)	51 (46)
Grade 3	46 (26)	52 (46)
Grade 4	7 (4)	9 (8)

\*\*Mann Whitney Test

+Fisher’s exact test

¶Chi-square test

Gestational Age (GA), birthweight (BW), Intravenous antibiotics (IVABx), parental nutrition (PN), Patent Ductus Arteriosus (PDA), High Frequency Oscillation ventilation (HFOV), Mean Airway Pressure (MAP), inspired oxygen (FiO<sub>2</sub>), oxygen saturations(SpO<sub>2</sub>), partial pressure of carbon dioxide on blood gas (pCO<sub>2</sub>), Haemoglobin (Hb), Pulmonary interstitial emphysema (PIE), chest xray (CXR)

Table 3 shows the results of the univariate and multivariate binary logistic regression analyses with unadjusted and adjusted odds ratios (OR). Those variables included in the multivariable analysis (p <0.2 on univariate) were the GA at birth, birthweight, presence of chorioamnionitis, number of failed extubations, age in days at starting dexamethasone, current weight, ventilation mode at time of dexamethasone, FiO<sub>2</sub> 24hrs prior to dexamethasone, MAP, PN use, feed type, last pH and pCO<sub>2</sub> on gas prior, PDA status, episodes of sepsis, airleak and CXR grade. Corrected GA at the time of starting dexamethasone was not included in the model because it was linearly correlated with age at stating dexamethasone so only one of these variables was included (i.e., age at stating dexamethasone).

The univariate analysis suggests that GA at birth was strongly protective with each additional gestational week leading to a 1.8 increase in the odds of successful extubation by 14 days (p<0.001). This was confirmed when adjusting for the other patient variables (OR=1.533; 95% CI: 1.122,2.096; p<0.01). BW, age in days and current weight at the time of dexamethasone were all strongly predictive of successful extubation in univariate analysis however after mutual adjustment these factors were no longer significant.

Several potentially important prognostic factors identified by the univariate analysis, could no longer be shown to be significant predictors when we adjusted for other factors. These include HFOV, PDA status and CXR grading of BPD.

Multivariable modelling revealed two other variables that remained significantly different once adjusting for all other variables. The predictive effects of FiO<sub>2</sub> and MAP remained significant even after adjusting for other important prognostic indicators. For every additional unit of average FiO<sub>2</sub> requirement in preceding 24 hours, there was an associated 6% decrease in the odds pf successful extubation by day 14 (OR=0.94, 95%CI: 0.921, 0.997; p<0.05) and higher MAP resulting in 0.76 times the odds in extubation (p<0.01).

**Table 3.** Unadjusted and adjusted odds ratios (OR) for odds of being *successfully extubated* by day 14 after starting dexamethasone.

Variable	Odds Ratio (Unadjusted)	Odds ratio (Adjusted)	Adjusted OR 95% CI
GA (weeks)	1.788***	1.533**	1.122, 2.096
Birth weight (100g)	1.427***	1.426	0.929, 2.190
Female	1.131		
Inborn	0.744		
Oligohydramnios	0.894		
Chorioamnionitis	0.529*	0.714	0.359, 1.418
Antenatal steroids <24hrs	χ <sup>2</sup> LRT = 2.573 0.618		

Variable	Odds Ratio (Unadjusted)	Odds ratio (Adjusted)	Adjusted OR 95% CI
completed	0.514		
> 7 days	1.313		
Postnatal Surfactant	0.776		
Failed Extubation Attempts	1.922**	0.833	0.357, 1.940
Duration of Dex Course (days)	1.004		
Days ventilated prior to dex	1.022+	1.026	0.958, 1.099
Age at starting dex (days)	1.070***	1.068	0.974, 1.170
Weight at starting dex (100g)	1.339***	0.956	0.698,1.310
IVABx at Dex	0.687		
Total Fluid Intake (mls/kg/day)	0.999		
Starting dose of Dexamethasone	2.097		
Average SpO2 24hr prior to Dex	1.118* (sats24beforeDEX?)	1.112	0.976, 1.266
Ventilation mode HFOV	0.369***	1.533	0.597,3.936
FiO2 24hrs prior to dex	0.939***	0.958*	0.921, 0.997
MAP (cmH2O)	0.759***	0.764**	0.634,0.921
TPN	0.790		
Enteral Feeding	$\chi^2$ LRT = 4.950+	$\chi^2$ LRT = 2.310	
NBM	0.215+	0.236	0.028, 2.024
Formula	1.505	0.656	0.169, 2.546
Last pH before starting Dex	10.63+	4.278	0.078,235.892
Last pCO2 before starting Dex	1.003		
Last Hb before starting Dex (g/L)	1.001		
PDA status	$\chi^2$ LRT=18.407***	$\chi^2$ LRT=5.582+	
Presumed open	0.935	0.802	0.218,2.944
Echo open	0.278***	0.523	0.199,1.372
Echo Closed	0.320**	0.312*	0.110,0.883
Sepsis	$\chi^2$ LRT=0.901		
before dex	1.011		
within 5 days of starting dex	0.482		
Airleaks	$\chi^2$ LRT=6.732+	$\chi^2$ LRT=0.768	
Pneumothorax	0.835	1.019	0.400,2.597
PIE	0.345*	0.672	0.211, 2.139
Both	1.809	1.676	0.218, 12.913
CXR findings- N (%)	$\chi^2$ LRT=16.693***	$\chi^2$ LRT=0.799	
Grade 3	0.382***	0.732	0.368,1.458
Grade 4	0.336*	0.894	0.223,3.584

\*\*\*p<0.001, \*\*p<0.01, \*p<0.05, + p<0.2

Gestational Age (GA), Intravenous antibiotics (IVABx), parental nutrition (PN), Patent Ductus Arteriosus (PDA), High Frequency Oscillation ventilation (HFOV), Mean Airway Pressure (MAP), fraction of inspired oxygen (FiO<sub>2</sub>), oxygen saturations(SpO<sub>2</sub>), partial pressure of carbon dioxide on blood gas (pCO<sub>2</sub>),Haemoglobin (Hb), Pulmonary interstitial emphysema (PIE), chest xray (CXR)

## DISCUSSION

In this study we investigated which clinical characteristics may be associated with successful extubation following the commencement of dexamethasone in less than 30 week GA neonates with BPD. Our analysis show that after we adjusted for the multiple factors measured, three factors remained as likely to be prognostically informative. These included less mature at birth, higher MAP, and greater FiO<sub>2</sub> requirement.

There are very few similar studies: most involving older patient cohorts and focus on long-term outcomes. Our study is the first looking specifically at extubation success and the occurrence of both modifiable and unmodifiable individual patient variables. Cuna<sup>17</sup> evaluated the outcomes of neonates with evolving BPD who were ventilator dependent and treated with systemic dexamethasone at either 14-28 days old vs 29-42 days old. They found that delaying dexamethasone had worse outcomes; it is difficult to compare Cuna's study to ours as both the patient cohort and the primary outcomes differ, and their data do not allow predicting successful extubation at the time of starting steroids.

A likely explanation as to why the individual variables affect extubation success is that they either increase the risk of BPD (younger GA) or are markers of the severity of BPD (MAP and FiO<sub>2</sub> requirement). Higher MAP and greater FiO<sub>2</sub> requirement will decrease the chance of successful extubation as it is these neonates that have more severe pulmonary inflammation and require higher tidal volumes and oxygen delivery for adequate ventilation and oxygenation. The trends in data (both Table 2 and Table 3 - unadjusted ORs) support this, as those not successfully extubated by day 14 had higher MAPs (13, IQR 11-14 cm H<sub>2</sub>O) and higher average FiO<sub>2</sub> requirements (0.40, IQR 0.33-0.48) compared to those successfully extubated MAP (11, range 10-12 cm H<sub>2</sub>O) and FiO<sub>2</sub> (0.35, range 0.30-0.39). These neonates were also less mature at birth putting them at greater risk of BPD. They also had a higher proportion of grade 3 or 4 CXR changes (66% vs 32%) and higher proportion on HFOV use (41% vs 21%). The higher proportion of neonates requiring HFOV in this study cohort is noteworthy, given that its use is predominantly as a rescue strategy once conventional ventilation was no longer adequate. Whilst we have identified variables associated with failing extubation, it is important to acknowledge which are potentially modifiable, and therefore which factors we as clinicians, can act on to maximise the chances of successful extubation in this high-risk population. Given the large variability of MAP and FiO<sub>2</sub> requirement we cannot provide cut-off values at which they are no longer negatively predictive of successful extubation, so clinical acumen is required. It is a balance between the risk and benefit of staying on the ventilator to achieve lung growth and potentially decrease FiO<sub>2</sub> and MAP requirements versus risking extubation failure and increasing the number of repeated ventilation courses which we know is detrimental.<sup>1</sup> It would be require a randomised controlled trial to investigate such strategies.

Another counter-intuitive finding is that we could not demonstrate the starting dose of dexamethasone to be associated with successful extubation. Having said this, the retrospective nature of this observational study means we were unable to systematically vary neither dose or duration independent of other clinical variables. Different clinicians made these decisions based on a variety of factors, several of which, were possibly not recorded in our dataset. To clarify this issue we would suggest performing a prospective study.

There were some limitations to this study. Its retrospective nature means that the reasoning for the timing of dexamethasone treatment is unknown. There may also have been a confounding effect in our study related to practice variation (across the ten-year period) in practices not related to dexamethasone prescription including but not limited to feeding methodology, medication types, parenteral nutrition usage, and some subtle changes to ventilation practices. It was not possible within the constraints of this dataset to control for these variables. The results may also not be generalizable to other neonatal units with different extubation practices and, given the complexity, a larger sample collected from across multiple neonatal units may be useful.

The strengths of this study include a comparatively large sample size and that as far as we know prescribing practices for dexamethasone remained consistent across the duration of the study. All neonates receiving systemic dexamethasone older than 7 days of age.<sup>9</sup> A potential decrease in confounding could be inferred from the reasonable sample size of our study allowing multivariable analysis to adjust for multiple confounding factors including GA, weight and postnatal age.

This study has established a number of factors present at the onset of the first course of dexamethasone are predictive of extubation success. However further work could be done: a more comprehensive multi-centre prospective study which would allow first, a better understanding of the suitability and utility in deferring steroid treatment, and second, the development of prognostic scoring models.

## CONCLUSIONS

Mechanically ventilated neonates born at less than 30 week GA, with evidence of BPD requiring systemic dexamethasone to facilitate extubation, have a reduced chance of successful extubation by day 14 if at the time of commencing steroids if they were less mature at birth, and had higher MAP and oxygen requirements at the time of starting dexamethasone.

## Acknowledgements

We thank Dr Adam Hoellering for his grading of the 287 chest xrays, and Dr David Cartwright for information gathered from NeoDATA.

## What is known about this topic;

1. BPD is the most common complication of extreme prematurity often requiring prolonged periods of mechanical ventilation
2. Systemic dexamethasone facilitates weaning of invasive ventilatory support by suppressing inflammation, improving lung compliance, and decreasing airway resistance
3. Steroids have documented side effects and should be reserved for neonates who are difficult to extubate from mechanical ventilation with the lowest cumulative dose given

## What this study adds;

Mechanically ventilated premature neonates have a reduced chance of successful extubation if at the time of commencing steroids they were less mature at birth, and had higher MAP and oxygen requirements

Birth weight and the weight at commencing steroids does not affect successful extubation following a dexamethasone course

## References

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