

Table 1 A. Characteristics of the 6680 neonates and use of sedative and analgesic drugs by ventilation groups§§

	Total n= 6680	Tracheal ventilation n=2142	Non invasive ventilation n=1496	Spontaneous ventilation n=3042	P value*
Patient Characteristics					
Gestational age- weeks					
Mean ± SD	35.0 ± 4.6	32.7 ± 5.2	33.8 ± 3.8	37.3 ± 3.1	<0.0001
Median (IQ)	35.6 (32.0-39.0)	32.1 (28.1-37.4)	33.6 (31.0-36.6)	37.9 (35.0-39.9)	<0.0001
24-29, no. (%)	1049 (15.7)	779 (36.4)	214 (14.3)	56 (1.8)	<0.0001**
30-32, no. (%)	1015 (15.2)	360 (16.8)	454 (30.3)	201 (6.6)	-
33-36, no. (%)	1864 (27.9)	389 (18.2)	486 (32.5)	989 (32.5)	-
37-42, no. (%)	2750 (41.2)	613 (28.6)	342 (22.9)	1795 (59.0)	-
Birth weight-grams					
Mean ± SD	2384 ± 1007	1947 ± 1034	2132 ± 891	2816 ± 855	<0.0001
Median (IQ)	2370 (1570-3170)	1740 (1000-2800)	1970 (1440-2720)	2870 (2140-3445)	<0.0001
Male, no. (%)	3775 (56.5)	1260 (58.8)	842 (56.3)	1673 (55)	0.10
Born in same hospital as NICU, no. (%)	5367 (80.3)	1460 (68.2)	1307 (87.4)	2600 (85.5)	<0.0001
Type of delivery- no. (%)					
Vaginal	3074 (46.2)	879 (41.3)	571 (38.2)	1624 (53.5)	<0.0001
Caesarean	3586 (53.8)	1249 (58.7)	923 (61.8)	1414 (46.5)	-
Age at admission - hours					
Mean ± SD	65.2 ± 244.3	84.1 ± 294	47.5 ± 224	60.6 ± 212	<0.0001
Median (IQ)	1.0 (0.3-12.1)	0.8 (0.3-8.3)	0.5 (0.2-1.7)	3.0 (0.4-26.8)	-
CRIB score†					
Mean ± SD	1.4 ± 2.5	3.3 ± 3.5	0.8 ± 1.5	0.4 ± 1.0	<0.0001
Median (IQ)	0 (0-2)	2 (1-5)	0 (0-1)	0 (0-0)	-
APGAR score at 5 min					
Mean ± SD	8.4 ± 1.9	7.4 ± 2.4	8.5 ± 1.4	9.0 ± 1.3	<0.0001
Median (IQ)	9 (8-10)	8 (6-9)	9 (8-10)	9 (9-10)	-
Already intubated at admission, no. (%)	1344 (20.1) ¶¶	1344 (62.7)	NA	NA	-
Died during study period, no. (%)	211 (3.2)	201 (9.4)	3 (0.2)	7 (0.2)	<0.0001
Duration of hospitalization- days					
Mean ± SD	11.9 ± 9.7	15.7 ± 10.2	14.2 ± 9.9	8.0 ± 7.4	<0.0001
Median (IQ)	8 (3-20)	14 (6-28)	11 (5-26)	5 (3-11)	<0.0001

Duration of Ventilation					
Tracheal Ventilation – hours ¶					
Mean ± SD	NA	115 ± 164	NA	NA	NA
Median (IQ)	NA	49 (14-130)	NA	NA	NA
Non-invasive ventilation – hours ¶¶					
Mean ± SD	NA	178 ± 197	92 ± 147	NA	NA
Median (IQ)	NA	84 (24-294)	34 (13-97)	NA	NA
Spontaneous ventilation – hours ¶¶					
Mean ± SD	NA	207 ± 192	249 ± 213	169 ± 179	NA
Median (IQ)	NA	138 (45-340)	173 (55-437)	103 (39-233)	NA
Use of sedative/analgesic drugs					
Mode of administration, no. (%)					
Any form‡	2294 (34.3)	1746 (81.5)	266 (17.8)	282 (9.3)	<0.0001***
Continuous only	309 (4.6)	294 (13.7)	5 (0.3)	10 (0.3)	-
Bolos only	936 (14.0)	451 (21.1)	247 (16.5)	238 (7.8)	-
Continuous and bolus	1049 (15.7)	1001 (46.7)	14 (0.9)	34 (1.1)	-
Category of analgesics or sedatives, no.(%)					
Opioid analgesics	1764 (26.4) §	1589 (74.2)	87 (5.8)	88 (2.9)	<0.0001
Sedative-Hypnotique	786 (11.8)	690 (32.2)	43 (2.8)	53 (1.7)	<0.0001
<i>Midazolam</i>	576 (8.6)	536 (25.0)	16 (1.1)	24 (0.8)	
<i>Barbiturates</i>	96 (1.4)	69 (3.2)	8 (0.5)	19 (0.6)	
<i>Other</i>	195 (2.9)	157 (7.3)	20 (1.3)	18 (0.6)	
General anesthetics	199 (3.0)	178 (8.3)	13 (0.9)	8 (0.3)	<0.0001
<i>Ketamine</i>	136 (2.0)	120 (5.6)	9 (0.6)	7 (0.2)	
<i>Propofol</i>	65 (1.0)	59 (2.8)	5 (0.3)	1 (0.03)	
<i>Inhalational anesthetics</i>	3 (0.04)	3 (0.1)	0 (0.0)	0 (0.0)	
Nonsteroidal anti-inflammatory drugs	920 (13.8)	544 (25.4)	173 (11.6)	203 (6.7)	<0.0001
<i>Acetaminophen</i>	904 (13.5)	530 (24.7)	172 (11.5)	202 (6.6)	
<i>Ibuprofen</i>	16 (0.2)	14 (0.7)	1 (0.1)	1 (0.1)	
Local anesthetics	26 (0.4)	21 (1.0)	2 (0.1)	3 (0.1)	<0.0001
Others	16 (0.2)	11 (0.5)	0 (0.0)	5 (0.2)	
Neuromuscular blockers	542 (8.1)	542 (25.3)	0 (0.0)	0 (0.0)	<0.0001
Pain assessment with a tool ††	2838 (42.7)	1250 (58.5)	672 (45.0)	916 (30.4)	<0.0001
Withdrawal syndrome diagnosed	94 (1.4)	69 (3.2)	4 (0.3)	21 (0.7)	<0.0001

*Comparisons of the three types of ventilation using chi square, ANOVA or Kruskal-Wallis statistics; **Chi square for distributions among all gestational ages classes within the three types of ventilation. ***Chi square for comparisons of different modes of administration among the three types of ventilation.

†The CRIB score is a measure of illness severity in neonates. It consists of 6 items collected in the first 12 hours after birth. It ranges from 0 to 23 where higher scores indicate higher clinical risk

¶¶ 26 infants were intubated immediately upon arrival in the unit and thus were included in this group

|| Data collection was stopped on the 28th day of hospitalization.

¶¶ For tracheal ventilation group, time on non-invasive ventilation (NIV) or spontaneous ventilation (SV) refers to NIV use or SV before tracheal intubation or after extubation. For NIV group, time on spontaneous ventilation refers to the periods of spontaneous ventilation before or after NIV use.

‡Continuous and/or bolus

|||Some patients received more than one type of analgesic or sedative

§From these 1764 neonates, 1707 (96.8%) received morphine (n=1016) and/or fentanyl (n=694) and/or sufentanil (n=227).

§§The highest level of ventilation during the study period classified patients into three groups: tracheal ventilation, non-invasive ventilation and spontaneous ventilation

†† Information available for 2138 neonates in the tracheal ventilation group, 1493 in the non-invasive ventilation group and 3017 in the spontaneous ventilation group

Abbreviations: NA= non applicable; SD: Standard Deviation; IQ: Interquartile

Table 1B. Characteristics of the 2064 neonates under 33 weeks and use of sedative and analgesic drugs by ventilation groups§§

	Total n= 2064	Tracheal ventilation n=1139	Non invasive ventilation n=668	Spontaneous ventilation n=257	P value*
Patient Characteristics					
Gestational age- weeks					
Mean ± SD	29.4 ± 2.5	28.4 ± 2.5	30.4 ± 1.9	30.9 ± 2.1	<0.0001
Median (IQ)	29.9 (27.4-31.6)	28.4 (26.4-30.4)	30.9 (29.4-32.0)	31.6 (30.0-32.3)	<0.0001
Birth weight-grams					
Mean ± SD	1269 ± 436	1131 ± 417	1419 ± 397	1490 ± 394	<0.0001
Median (IQ)	1230 (920-1580)	1045 (801-1395)	1411 (1116-1718)	1500 (1255-1755)	<0.0001
Male, no. (%)	1154 (55.9)	674 (59.2)	352 (52.7)	128 (49.8)	0.009
Born in same hospital as NICU, no. (%)	1681 (81.4)	909 (79.8)	590 (88.3)	182 (70.8)	<0.0001
Type of delivery- no. (%)					
Vaginal	708 (34.4)	401 (35.3)	204 (30.6)	1624 (53.5)	0.015
Caesarean	1352 (65.6)	735 (64.7)	463 (69.4)	1414 (46.5)	-
Age at admission - hours					
Mean ± SD	125.6 ± 395.1	110.9 ± 373.1	79.2 ± 312.4	311.5 ± 586.4	<0.0001
Median (IQ)	0.5 (0.3-1.8)	0.5 (0.3-2.0)	0.4 (0.2-0.9)	0.8 (0.3-273.5)	-
CRIB score†					
Mean ± SD	2.5 ± 3.3	3.8 ± 3.7	1.1 ± 1.7	1.0 ± 1.8	<0.0001
Median (IQ)	1 (0-4)	2 (1-6)	1 (0-1)	0 (0-1)	-
APGAR score at 5 min					
Mean ± SD	8.0 ± 1.9	7.4 ± 2.1	8.6 ± 1.3	9.0 ± 1.2	<0.0001
Median (IQ)	8 (7-9)	8 (6-9)	9 (8-9)	9 (9-10)	-
Already intubated at admission, no. (%)	811 (39.3) ¶¶	811 (71.2)	NA	NA	-
Died during study period, no. (%)	139 (6.7)	139 (12.2)	0 (0.0)	0 (0.0)	<0.0001
Duration of hospitalization- days					
Mean ± SD	19.4 ± 9.8	19.8 ± 9.9	19.4 ± 9.6	17.3 ± 9.4	0.001
Median (IQ)	25 (10-28)	28 (10-28)	25 (9-28)	18 (8-28)	<0.0001
Duration of Ventilation					
Tracheal Ventilation – hours ¶					
Mean ± SD	NA	147 ± 194	NA	NA	NA
Median (IQ)	NA	58 (18-182)	NA	NA	NA
Non-invasive ventilation – hours ¶					

Mean ± SD	NA	243 ± 208	155 ± 192	NA	NA
Median (IQ)	NA	181 (53-429)	70 (25-188)	NA	NA
Spontaneous ventilation – hours ¶					
Mean ± SD	NA	269 ± 215	341 ± 227	394 ± 227	NA
Median (IQ)	NA	221 (67-472)	359 (110-565)	417 (171-649)	NA
Use of sedative/analgesic drugs					
Mode of administration, no. (%)					
Any form‡	1031 (50.0)	881 (77.3)	124 (18.6)	26 (10.1)	<0.0001**
Continuous only	155 (7.5)	154 (13.5)	1 (0.1)	0 (0.0)	-
Bolos only	420 (20.3)	279 (24.5)	119 (17.8)	22 (8.6)	-
Continuous and bolus	456 (22.1)	448 (39.3)	4 (0.6)	4 (1.6)	-
Category of analgesics or sedatives, no.(%)					
Opioid analgesics	851 (41.2) §	796 (69.9)	49 (7.3)	6 (2.3)	<0.0001
Sedative-Hypnotic	272 (13.2)	255 (22.4)	15 (2.2)	2 (0.8)	<0.0001
<i>Midazolam</i>	197 (9.5)	190 (16.7)	5 (0.7)	2 (0.8)	
<i>Barbiturates</i>	16 (0.8)	12 (1.1)	4 (0.6)	0 (0.0)	
<i>Other</i>	63 (3.1)	58 (5.1)	5 (0.7)	0 (0.0)	
General anesthetics	82 (4.0)	72 (6.3)	10 (1.5)	0 (0.0)	<0.0001
<i>Ketamine</i>	40 (1.9)	33 (2.9)	7 (1.0)	0 (0.0)	
<i>Propofol</i>	42 (2.0)	38 (3.3)	4 (0.6)	0 (0.0)	
<i>Inhalational anesthetics</i>	2 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	
Nonsteroidal anti-inflammatory drugs	341 (16.5)	243 (21.3)	74 (11.1)	24 (9.3)	<0.0001
<i>Acetaminophen</i>	326 (15.8)	229 (20.1)	73 (10.9)	24 (9.3)	
<i>Ibuprofen</i>	15 (0.7)	14 (1.2)	1 (0.1)	0 (0.0)	
Local anesthetics	8 (0.4)	7 (0.6)	0 (0.0)	1 (0.4)	0.13
Others	2 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	
Neuromuscular blockers	259 (12.5)	259 (22.7)	0 (0.0)	0 (0.0)	<0.0001
Pain assessment with a tool ††	1136 (55.3)	682 (60.1)	342 (51.4)	112 (43.8)	<0.0001
Withdrawal syndrome diagnosed	15 (0.7)	13 (1.1)	2 (0.3)	0 (0.0)	0.49

*Comparisons of the three types of ventilation using chi square, ANOVA or Kruskal-Wallis statistics; **Chi square for comparisons of different modes of administration among the three types of ventilation.

†The CRIB score is a measure of illness severity in neonates. It consists of 6 items collected in the first 12 hours after birth. It ranges from 0 to 23 where higher scores indicate higher clinical risk

¶¶ 16 infants were intubated immediately upon arrival in the unit and thus were included in this group

|| Data collection was stopped on the 28th day of hospitalization.

¶¶ For tracheal ventilation group, time on non-invasive ventilation (NIV) or spontaneous ventilation (SV) refers to NIV use or SV before tracheal intubation or after extubation. For NIV group, time on spontaneous ventilation refers to the periods of spontaneous ventilation before or after NIV use.

‡Continuous and/or bolus

|||Some patients received more than one type of analgesic or sedative

§From these 851 neonates, 821 (96.5%) received morphine (n=473) and/or fentanyl (n=344) and/or sufentanil (n=104).

§§The highest level of ventilation during the study period classified patients into three groups: tracheal ventilation , non-invasive ventilation and spontaneous ventilation

††Information available for 1135 neonates in the tracheal ventilation group, 665 in the non-invasive ventilation group and 256 in the spontaneous ventilation group

Abbreviations: NA= non applicable; SD: Standard Deviation; IQ: Interquartile

Table 2A. Logistic regression models of factors associated with the use of any sedation/analgesia and the use of opioids, sedatives-hypnotics or general anesthetics in all neonates and tracheally ventilated neonates**

	All neonates (N=6680)					Tracheally ventilated neonates (N=2142)				
	Number of neonates	Any sedation/analgesia		Opioids, sedatives-hypnotics or general anesthetics §		Number of neonates	Any sedation/analgesia		Opioids, sedatives-hypnotics or general anesthetics §	
		Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value		Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Sex										
Male	3563	1.00*		1.00*		1180	1.00*		1.00*	
Female	2744	0.86 (0.74-1.00)	0.06	0.94 (0.79-1.12)	0.49	824	0.85 (0.66-1.09)	0.21	0.82 (0.65-1.04)	0.10
Gestational age (weeks)										
37-42	2604	1.00*		1.00*		574	1.00*		1.00*	
33-36	1765	0.61 (0.50-0.74)	<0.0001	0.76 (0.60-0.95)	0.019	372	0.58 (0.39-0.87)	0.009	0.75 (0.51-1.09)	0.13
30-32	971	0.60 (0.47-0.76)	<0.0001	0.62 (0.47-0.82)	0.001	343	0.48 (0.32-0.74)	0.001	0.50 (0.34-0.73)	<0.0001
24-29	967	0.47 (0.36-0.61)	<0.0001	0.51 (0.39-0.67)	<0.0001	715	0.59 (0.38-0.90)	0.014	0.65 (0.45-0.95)	0.025
Age at admission (hours)										
> 168	459	1.00*		1.00*		172	1.00*		1.00*	
73-168	245	0.68 (0.44-1.06)	0.09	0.88 (0.52-1.51)	0.66	46	1.04 (0.20-5.51)	0.96	1.42 (0.36-5.59)	0.62
25-72	470	0.64 (0.44-0.94)	0.022	0.85 (0.53-1.38)	0.51	88	0.65 (0.23-1.82)	0.41	0.82 (0.36-1.88)	0.65
7-24	711	0.60 (0.42-0.85)	0.004	0.78 (0.51-1.18)	0.24	213	0.50 (0.20-1.24)	0.14	0.79 (0.39-1.61)	0.52
<7	4422	0.40 (0.30-0.53)	<0.0001	0.39 (0.28-0.54)	<0.0001	1485	0.17 (0.08-0.38)	<0.0001	0.28 (0.16-0.51)	<0.0001
IUGR										
No	5208	1.00*		1.00*		1680	1.00*		1.00*	
Yes	1099	0.83 (0.67-1.03)	0.09	0.90 (0.71-1.16)	0.42	324	0.70 (0.49-0.99)	0.044	0.80 (0.58-1.01)	0.17
Respiratory distress syndrome										
No	4432	1.00*		1.00*		1029	1.00*		1.00*	
Yes	1875	0.75 (0.62-0.90)	0.002	1.06 (0.87-1.30)	0.56	975	0.70 (0.52-0.95)	0.021	0.88 (0.67-1.17)	0.38
CRIB score†	6307	1.25 (1.19-1.31)	<0.0001	1.26 (1.21-1.32)	<0.0001	2004	1.33 (1.25-1.42)	<0.0001	1.31 (1.24-1.39)	<0.0001
APGAR at 1 min§§	6307	1.0 (1.0-1.1)	0.15	1.1 (1.0-1.1)	0.009	2004	1.0 (1.0-1.1)	0.07	1.0 (1.0-1.1)	0.25
Already intubated at admission		NA		NA						
No						731	1.00*		1.00*	
Yes						1273	0.18 (0.13-0.26)	<0.0001	0.21 (0.15-0.28)	<0.0001
Respiratory support‡										
Spontaneous ventilation	2863	1.00*		1.00*			NA		NA	
Non-invasive ventilation	1440	2.84 (2.30-3.51)	<0.0001	2.83 (2.13-3.76)	<0.0001					
Tracheal ventilation	2004	43.73 (35.03-54.59)	<0.0001	79.27 (60.55-103.77)	<0.0001					
Pain assessment										
No	3656	1.00*		1.00*		848	1.00*		1.00*	
Yes	2651	1.78 (1.53-2.07)	<0.0001	1.74 (1.47-2.07)	<0.0001	1156	1.82 (1.41-2.35)	<0.0001	1.84 (1.45-2.33)	<0.0001
Model area under the receiver operating characteristic curve¶		0.893 (0.884-0.901)		0.926 (0.919-0.934)			0.797 (0.773-0.821)		0.777 (0.753-0.802)	

Optimism in apparent performance¶¶		<i>0.0001487</i>	<i>0.0000991</i>		<i>0.0003624</i>	<i>0.0001021</i>
Optimism-Corrected area¶¶		<i>0.893 (0.884-0.902)</i>	<i>0.926 (0.919-0.934)</i>		<i>0.797 (0.773-0.821)</i>	<i>0.777 (0.753-0.802)</i>

** Adjusted on centers. P-values and confidence intervals were adjusted using a robust sandwich estimator.

|| Any form of sedation analgesia includes opioids, sedatives-hypnotics, general anesthetics, Nonsteroidal Anti-inflammatory Drugs, local anesthetics and others.

§ Opioids, sedatives-hypnotics or general anesthetics drugs include all opioids, ketamine, benzodiazepines, propofol, barbiturates, chloral hydrate and other sedatives. Comparison against no analgesia/sedation or other types of analgesia.

*Reference category

†Odds ratio per point increase in CRIB score. The CRIB score is a measure of illness severity in neonates. It consists of 6 items collected in the first 12 hours after birth. It ranges from 0 to 23 where higher scores indicate higher clinical risk.

‡Patients were classified in 3 groups according to the highest level of ventilation they received during the study period

¶ Area with 95% confidence interval (0.5 = no predictive value; 1.0 = perfect prediction)

¶¶An internal validation of the model was performed using a bootstrap approach (1000 samples)

§§ Odds ratio per point increase in APGAR score. This score ranges from 0 to 10

Abbreviations: CI: Confidence interval; SD: Standard Deviation ; NA: Non applicable; IUGR: intrauterine growth retardation

Table 2B. Logistic regression models of factors associated with the use of opioids, the use of sedatives-hypnotics and the use of general anesthetics in tracheally ventilated neonates**

	Tracheally ventilated neonates (N=2142)						
	Number of neonates	Opioids Odds ratio (95% CI) P value		Sedatives-hypnotics Odds ratio (95% CI) P value		General anesthetics Odds ratio (95% CI) P value	
Sex							
Male	1180	1.00*		1.00*		1.00*	
Female	824	0.74 (0.60-0.93)	0.008	0.91 (0.73-1.12)	0.36	1.06 (0.75-1.50)	0.74
Gestational age (wks)							
37-42	574	1.00*		1.00*		1.00*	
33-36	372	0.91 (0.64-1.29)	0.59	0.62 (0.46-0.83)	0.001	0.68 (0.40-1.15)	0.15
30-32	343	0.55 (0.39-0.79)	0.001	0.32 (0.23-0.46)	<0.0001	0.65 (0.37-1.13)	0.13
24-29	715	0.69 (0.49-0.99)	0.041	0.29 (0.21-0.40)	<0.0001	0.87 (0.53-1.44)	0.60
Age at admission (h)							
> 168	172	1.00*		1.00*		1.00*	
73-168	46	1.33 (0.39-4.50)	0.64	0.65 (0.33-1.28)	0.21	1.21 (0.46-3.20)	0.70
25-72	88	0.68 (0.32-1.43)	0.30	0.38 (0.22-0.65)	0.0004	0.74 (0.30-1.87)	0.53
7-24	213	0.84 (0.44-1.61)	0.60	0.48 (0.31-0.74)	0.001	0.60 (0.29-1.23)	0.16
<7	1485	0.32 (0.19-0.55)	<0.0001	0.32 (0.23-0.46)	<0.0001	0.43 (0.25-0.74)	0.002
IUGR							
No	1680	1.00*		1.00*		1.00*	
Yes	324	0.70 (0.52-0.95)	0.021	1.23 (0.94-1.61)	0.14	1.56 (1.03-2.37)	0.035
Respiratory distress syndrome							
No	1029	1.00*		1.00*		1.00*	
Yes	975	0.86 (0.67-1.12)	0.28	0.77 (0.60-0.98)	0.04	0.77 (0.51-1.17)	0.22
CRIB score†	2004	1.31 (1.24-1.37)	<0.0001	1.13 (1.10-1.17)	<0.0001	1.03 (0.98-1.09)	0.22
APGAR at 1 min§§	2004	1.04 (0.99-1.08)	0.09	1.04 (0.99-1.08)	0.09	0.98 (0.91-1.05)	0.60
Already intubated at admission							
No	731	1.00*		1.00*		1.00*	
Yes	1273	0.35 (0.27-0.46)	<0.0001	0.83 (0.66-1.04)	0.11	0.30 (0.20-0.44)	<0.0001
Pain assessment							
No	848	1.00*		1.00*		1.00*	
Yes	1156	1.73 (1.39-2.16)	<0.0001	1.80 (1.45-2.23)	<0.0001	2.63 (1.76-3.92)	<0.0001
Model area under the receiver operating characteristic curve¶		0.753 (0.729-0.777)		0.731 (0.706-0.755)		0.741 (0.701-0.780)	
Optimism in apparent performance¶¶		-0.0000247		-0.0003018		0.0004471	
Optimism-Corrected area¶¶¶		0.753 (0.729-0.777)		0.730 (0.706-0.755)		0.741 (0.701-0.781)	

** Adjusted on centers. P-values and confidence intervals were adjusted using a robust sandwich estimator.

*Reference category

†Odds ratio per point increase in CRIB score. The CRIB score is a measure of illness severity in neonates. It consists of 6 items collected in the first 12 hours after birth. It ranges from 0 to 23 where higher scores indicate higher clinical risk.

‡Patients were classified in 3 groups according to the highest level of ventilation they received during the study period

¶ Area with 95% confidence interval (0.5 = no predictive value; 1.0 = perfect prediction)

¶¶An internal validation of the model was performed using a bootstrap approach (1000 samples)

§§ Odds ratio per point increase in APGAR score. This score ranges from 0 to 10

Abbreviations: CI: Confidence interval; SD: Standard Deviation ; IUGR: intrauterine growth retardation

Table 3. Univariate analysis and multivariable linear model of factors associated with longer duration of tracheal ventilation

	Number of neonates	Univariate analysis		Number of neonates	Linear model **	
		Mean (SD) duration of tracheal ventilation, h	P value		B (95% CI)	P value
Sex						
Male	1260	118.99 (166.62)	0.17	1180	1.00*	0.13
Female	880	109.00 (159.87)		824	-9.84 (6.49)	
Gestational age (weeks)			<0.0001			
37-42	613	76.76 (106.77)		574	1.00*	
33-36	389	81.10 (115.34)		372	17.50 (9.94)	0.08
30-32	360	60.53 (99.67)		343	18.01 (10.84)	0.10
24-29	779	187.63 (213.62)		715	100.80 (9.76)	<0.0001
Age at admission (hours)			0.013			
> 168	224	141.75 (178.97)		172	1.00*	
73-168	59	143.35 (164.62)		46	19.03 (23.74)	0.42
25-72	99	80.13 (115.31)		88	-11.91 (19.24)	0.54
7-24	231	117.50 (150.35)		213	9.60 (15.19)	0.53
<7	1529	112.02 (166.15)		1485	-11.29 (12.16)	0.35
Born in same hospital as NICU			0.81			
No	682	116.37 (150.87)				
Yes	1460	114.53 (170.15)				
CRIB score†	2057	0.307‡	<0.0001	2004	6.79 (1.08)	<0.0001
APGAR at 1 min§§	2088	-0.139‡	<0.0001	2004	-2.62 (1.26)	0.037
IUGR			0.001			
No	1785	109.73 (157.70)		1680	1.00*	
Yes	351	141.94 (191.04)	324	23.74 (8.79)	0.007	
Respiratory distress syndrome			0.001			
No	1125	103.85 (147.60)		1029	1.00*	
Yes	1017	127.57 (180.09)	975	7.56 (7.89)	0.34	
Already intubated at admission			<0.0001			
No	766	78.72 (109.89)		731	1.00*	
Yes	1376	135.37 (184.73)	1273	42.22 (7.64)	<0.0001	
Opioids, sedatives-hypnotics or general anesthetics use §			<0.0001			
No	468	39.79 (94.71)		445	1.00*	
Yes	1674	136.17 (173.14)	1559	96.47 (8.36)	<0.0001	
Pain assessment			0.002			
No	888	101.95 (159.86)		848	1.00*	
Yes	1250	123.85 (166.09)	1156	28.36 (8.11)	0.0005	

** Adjusted on countries. P-values were adjusted using a robust sandwich estimator

*Reference category

||Unless indicated otherwise

‡ Pearson correlation with duration of tracheal ventilation

† The CRIB score is a measure of illness severity in neonates. It consists of 6 items collected in the first 12 hours after birth. It ranges from 0 to 23 where higher scores indicate higher clinical risk.

§ Opioids, sedatives-hypnotics or general anesthetics drugs include all opioids, ketamine, benzodiazepines, propofol, barbiturates, chloral hydrate and other sedatives

§§ APGAR score ranges from 0 to 10

Abbreviations: CI: Confidence interval; SD: Standard Deviation ; NA: Non applicable; IUGR: intrauterine growth retardation