

Figure S1. Flow chart of inclusions

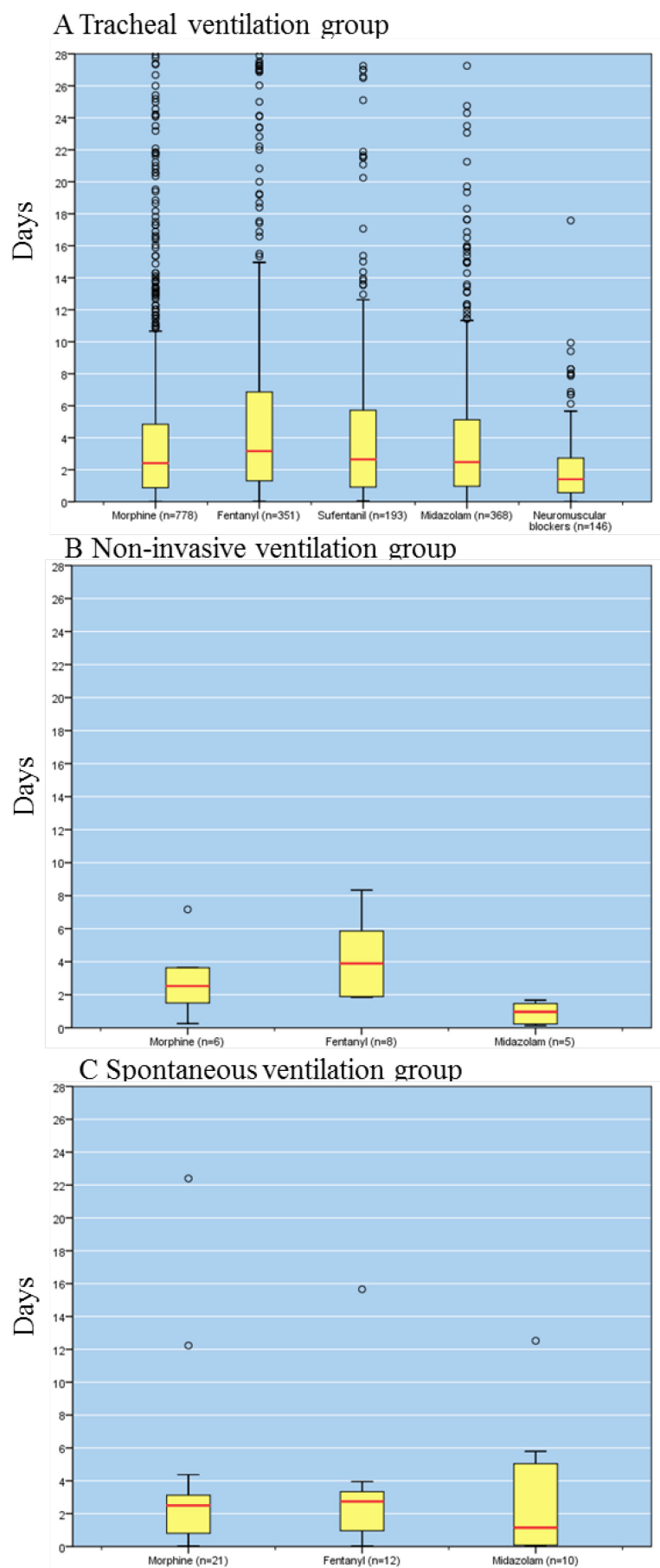
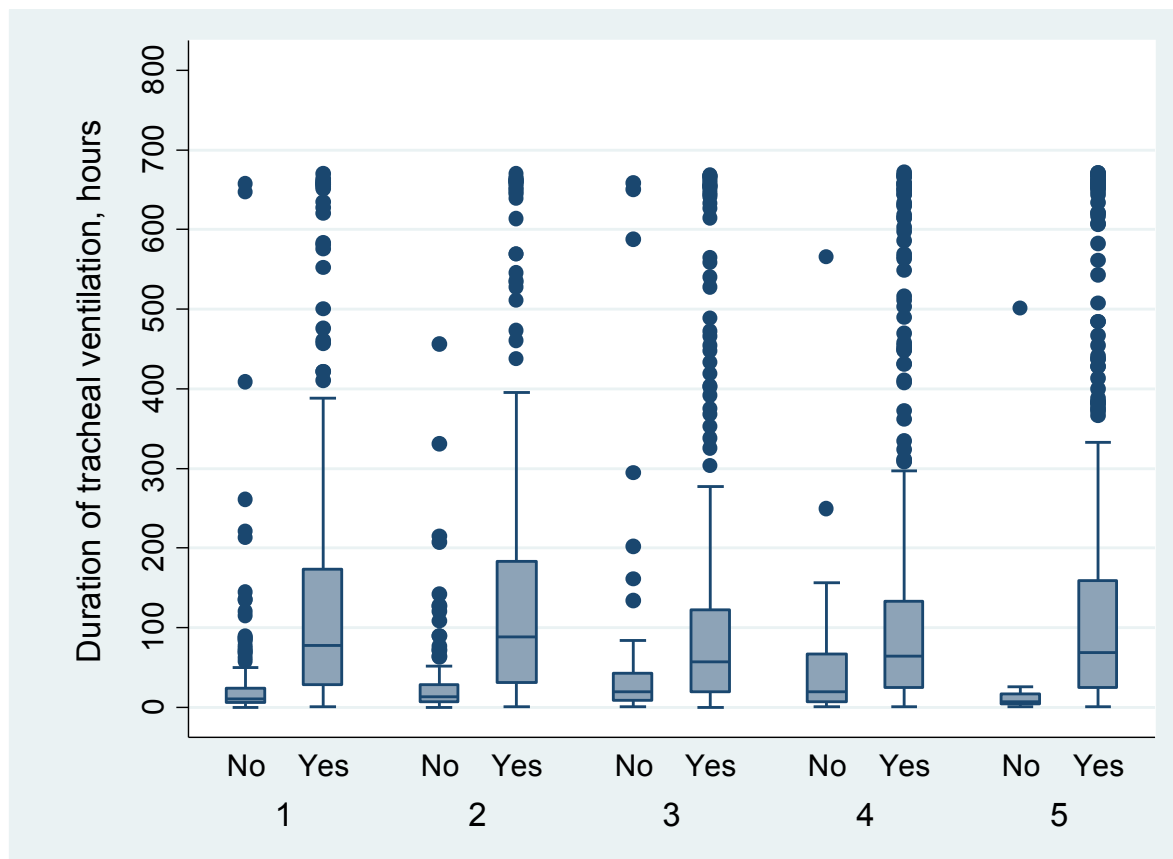


Fig. S2. Length of administration of morphine, fentanyl, sufentanil, midazolam, and neuromuscular blockers according to type of ventilation, showing box-plots for those who received these drugs in continuous infusion



Use of opioids and/or sedatives-hypnotics and/or general anesthetics by propensity-score quintiles

Figure S3. Median and interquartiles duration of tracheal ventilation in the 5 strata defined by the propensity score quintiles according to whether they received opioids and/or sedatives-hypnotics and/or general anesthetics. Comparisons of the subgroups with (Yes) and without (No) opioids and/or sedatives-hypnotics and/or general anesthetics use showed p values <0.001

Table S1. Participating Neonatal ICUs, patients enrolled, and ventilation groups by country

Countries				Patient enrollment			Type of ventilation for included patients ^c		
	Number of births in 2012 ^a	Number of Eligible NICUs in the country ^b	Number of participating NICUs	Number of patients eligible ^c	Number enrolled (rate of enrollment)	Number enrolled / 10000 births ^d	Tracheal ventilation N (%)	Non-invasive ventilation N (%)	Spontaneous ventilation N (%)
United Kingdom	812970	125	66	2768	2691 (97.2)	33.10	713 (26.5%)	438 (16.3%)	1540 (57.2%)
France	792000	60	34	929	916 (98.6)	11.57	497 (54.3%)	225 (24.6%)	194 (21.2%)
Spain	456778	40	30	496	468 (94.4)	10.25	202 (43.2%)	149 (31.8%)	117 (25.0%)
Greece	104000	23	13	455	455 (100.0)	43.75	126 (27.7%)	60 (13.2%)	269 (59.1%)
Italy	546607	90	28	468	422 (90.2)	7.72	131 (31.0%)	150 (35.5%)	141 (33.4%)
Norway	60255	16	16	477	334 (70.0)	55.43	35 (10.5%)	94 (28.1%)	205 (61.4%)
Portugal	89841	18	14	240	236 (98.3)	26.27	55 (23.3%)	54 (22.9%)	127 (53.8%)
Netherland	175457	10	5	208	208 (100.0)	11.85	69 (33.2%)	68 (32.7%)	71 (34.1%)
Finland	59493	6	6	217	201 (92.6)	33.79	52 (25.9%)	45 (22.4%)	104 (51.7%)
Sweden	113177	15	6	226	160 (70.8)	14.14	38 (23.8%)	47 (29.4%)	75 (46.9%)
Belgium	127000	19	4	130	128 (98.5)	10.08	37 (28.9%)	51 (39.8%)	40 (31.3%)
Germany	671000	160	4	127	126 (99.2)	1.88	29 (23.0%)	17 (13.5%)	80 (63.5%)
Cyprus	9622	1	1	84	84 (100.0)	87.30	41 (48.8%)	11 (13.1%)	32 (38.1%)
Poland	386257	41	8	83	83 (100.0)	2.15	50 (60.2%)	25 (30.1%)	8 (9.6%)
Austria	78952	13	4	73	73 (100.0)	9.25	22 (30.1%)	32 (43.8%)	19 (26.0%)
Lithuania	30459	2	1	45	45 (100.0)	14.77	23 (51.1%)	21 (46.7%)	1 (2.2%)
Malta	4130	1	1	28	28 (100.0)	67.80	5 (17.9%)	5 (17.9%)	18 (64.3%)
Estonia	14056	2	2	22	22 (100.0)	15.65	17 (77.3%)	4 (18.2%)	1 (4.5%)
TOTAL	4532054	642	243	7076	6680 (94.4)	14.74	2142 (32.1%)	1496 (22.4%)	3042 (45.5%)

^aInstitut National Etudes démographiques (www.ined.fr); ^bfulfilling participation criteria; ^cin participating units; ^dbirths in the country

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

Table S2. List of all opioids, sedatives-hypnotics, general anesthetics, and NSAIDs, local anesthetics and others used in each of the ventilation groups

	Tracheal ventilation (n=2142)				Non Invasive ventilation (n=1496)				Spontaneous ventilation (n=3042)			
	Bolus only N (%)	Continuous only N (%)	Continuous and bolus N (%)	TOTAL N (%)	Bolus only N (%)	Continuous only N (%)	Continuous and bolus N (%)	TOTAL N (%)	Bolus only N (%)	Continuous only N (%)	Continuous and bolus N (%)	TOTAL N (%)
Opioid analgesics												
<i>Morphine</i>	145 (6.8)	361 (16.9)	417 (19.5)	923 (43.1)	31 (2.1)	5 (0.3)	1 (0.1)	37 (2.5)	35 (1.2)	14 (0.5)	7 (0.2)	56 (1.8)
<i>Fentanyl</i>	278 (13.0)	141 (6.6)	210 (9.8)	629 (29.4)	33 (2.2)	5 (0.3)	3 (0.2)	41 (2.7)	12 (0.4)	7 (0.2)	5 (0.2)	24 (0.8)
<i>Sufentanil</i>	27 (1.3)	101 (4.7)	92 (4.3)	220 (10.3)	2 (0.1)	-	-	2 (0.1)	5 (0.2)	-	-	5 (0.2)
<i>Nalbuphine</i>	39 (1.8)	16 (0.7)	12 (0.6)	67 (3.1)	6 (0.4)	-	2 (0.1)	8 (0.5)	4 (0.1)	-	2 (0.1)	6 (0.2)
<i>Codeine</i>	1 (0.05)	-	-	1 (0.05)	-	-	-	-	1 (0.03)	-	-	1 (0.03)
<i>Oxycodone</i>	9 (0.4)	-	-	9 (0.4)	-	-	-	-	-	-	-	-
<i>Alfentanil</i>	7 (0.3)	-	-	7 (0.3)	-	-	-	-	-	-	-	-
<i>Remifentanyl</i>	5 (0.2)	5 (0.2)	-	10 (0.5)	1 (0.1)	-	-	1 (0.1)	-	-	-	-
<i>Piritramide</i>	1 (0.05)	-	-	1 (0.05)	-	-	-	-	-	-	-	-
<i>Tramadol</i>	-	-	-	-	1 (0.1)	-	-	1 (0.1)	1 (0.03)	-	-	1 (0.03)
<i>Pethidine</i>	4 (0.2)	-	-	4 (0.2)	-	-	-	-	-	-	-	-
<i>Fentanyl+</i> <i>Levobupivacaine</i>	-	-	-	-	-	-	-	-	-	1 (0.03)	-	1 (0.03)
General Anesthetics												
<i>Propofol</i>	59 (2.8)	-	-	59 (2.8)	5 (0.3)	-	-	5 (0.3)	1 (0.03)	-	-	1 (0.03)
<i>Ketamine</i>	29 (1.4)	86 (4.0)	5 (0.2)	120 (5.6)	9 (0.6)	-	-	9 (0.6)	7 (0.2)	-	-	7 (0.2)
<i>Sevoflurane</i>	-	2 (0.1)	-	2 (0.1)	-	-	-	-	-	-	-	-
<i>Xenon inhaled</i>	-	1 (0.05)	-	1 (0.05)	-	-	-	-	-	-	-	-
Sedatives-Hypnotics												
<i>Midazolam</i>	168 (7.8)	176 (8.2)	192 (9.0)	536 (25.0)	11 (0.7)	3 (0.2)	2 (0.1)	16 (1.1)	14 (0.5)	6 (0.2)	4 (0.1)	24 (0.8)
<i>Diazepam</i>	28 (1.3)	-	-	28 (1.3)	2 (0.1)	1 (0.1)	-	3 (0.2)	1 (0.03)	-	-	1 (0.03)
<i>Lorazepam</i>	4 (0.2)	-	-	4 (0.2)	1 (0.1)	-	-	1 (0.1)	-	-	-	-
<i>Pentobarbital</i>	3 (0.1)	-	-	3 (0.1)	-	-	-	-	-	-	-	-
<i>Clorazepate</i>	2 (0.1)	-	-	2 (0.1)	2 (0.1)	-	-	2 (0.1)	-	-	-	-
<i>Clonazepam</i>	2 (0.1)	4 (0.2)	-	6 (0.3)	-	-	-	-	-	-	-	-
<i>Lormetazepam</i>	1 (0.05)	-	-	1 (0.05)	-	-	-	-	-	-	-	-
<i>Delorazepam</i>	1 (0.05)	-	-	1 (0.05)	-	-	-	-	-	-	-	-
<i>Alprazolam</i>	1 (0.05)	-	-	1 (0.05)	-	-	-	-	-	-	-	-
<i>Phenobarbital</i>	53 (2.5)	-	1 (0.05)	54 (2.5)	7 (0.5)	-	-	7 (0.5)	17 (0.6)	-	2 (0.1)	19 (0.6)
<i>Penthotal</i>	16 (0.7)	1 (0.05)	-	17 (0.8)	1 (0.1)	-	-	1 (0.1)	-	-	-	-
<i>Pentobarbital</i>	3 (0.1)	-	-	3 (0.1)	-	-	-	-	-	-	-	-

<i>Chloral hydrate</i>	83 (3.9)	-	-	83 (3.9)	17 (1.1)	-	-	17 (1.1)	13 (0.4)	-	-	13 (0.4)
<i>Paraldehyde</i>	1 (0.05)	-	-	1 (0.05)	-	-	-	-	-	-	-	-
<i>Sodium gamma-oxybutyrate</i>	1 (0.05)	-	-	1 (0.05)	-	-	-	-	-	-	-	-
<i>Clonidine</i>	11 (0.5)	29 (1.4)	5 (0.2)	45 (2.1)	-	-	-	-	2 (0.1)	2 (0.1)	-	4 (0.1)
Nonsteroidal Anti-inflammatory Drugs, local anesthetics and others												
<i>Acetaminophen</i>	530 (24.7)	-	-	530 (24.7)	172 (11.5)	-	-	172 (11.5)	202 (6.6)	-	-	202 (6.6)
<i>Ibuprofen</i>	14 (0.7)	-	-	14 (0.7)	1 (0.1)	-	-	1 (0.1)	1 (0.03)	-	-	1 (0.03)
<i>Phloroglucinol</i>	3 (0.1)	-	-	3 (0.1)	-	-	-	-	1 (0.03)	-	-	1 (0.03)
<i>Phenytoin</i>	2 (0.1)	-	-	2 (0.1)	-	-	-	-	3 (0.1)	-	-	3 (0.1)
<i>Metamizole</i>	4 (0.2)	1 (0.05)	-	5 (0.2)	1 (0.1)	-	-	1 (0.1)	3 (0.1)	-	-	3 (0.1)
<i>Lidocaine</i>	8 (0.4)	-	-	8 (0.4)	2 (0.1)	-	-	2 (0.1)	-	-	-	-
<i>Chlorpromazine</i>	-	-	-	-	-	-	-	-	3 (0.1)	-	-	3 (0.1)
<i>Levetiracetam</i>	-	-	-	-	-	-	-	-	1 (0.03)	-	-	1 (0.03)
<i>Levomepromazine</i>	1 (0.05)	-	-	1 (0.05)	-	-	-	-	-	-	-	-
<i>Ropivacaine</i>	2 (0.1)	1 (0.05)	-	3 (0.1)	-	-	-	-	-	-	-	-
<i>Bupivacaine</i>	2 (0.1)	8 (0.4)	-	10 (0.5)	-	-	-	-	-	3 (0.1)	-	3 (0.1)
<i>Alimemazine</i>	4 (0.2)	-	-	4 (0.2)	-	-	-	-	-	-	-	-

- indicates zero

Table S3A. Use of main analgesics, sedatives-hypnotics and neuromuscular blockers, by country, in 2142 neonates who received tracheal ventilation

Country	Neonates with S/A n (%)	Morphine n (%)*	Fentanyl n (%)*	Sufentanil n (%)*	Ketamine n(%)*	Midazolam n (%)*	Propofol n(%)*	Chloral hydrate n (%)*	Neuromuscul ar blockers n (%)*	Acetaminoph en n (%)*
Austria	19/22 (86.4)	5 (26.3)	12 (63.2)	-	4 (21.1)	6 (31.6)	-	5 (26.3)	3 (15.8)	7 (36.8)
Belgium	34/37 (91.9)	13 (38.2)	21 (61.8)	-	-	1 (2.9)	5 (14.7)	1 (2.9)	14 (41.2)	10 (29.4)
Cyprus	40/41 (97.6)	40 (100.0)	-	-	-	-	-	-	11 (27.5)	-
Estonia	17/17 (100.0)	1 (5.9)	12 (70.6)	-	-	10 (58.8)	-	-	1 (5.9)	8 (47.1)
Finland	48/52 (92.3)	14 (29.2)	22 (45.8)	-	6 (12.5)	8 (16.7)	2 (4.2)	-	17 (35.4)	39 (81.3)
France	377/497 (75.9)	97 (25.7)	58 (15.4)	198 (52.5)	60 (15.9)	223 (59.2)	8 (2.1)	-	33 (8.8)	165 (43.8)
Germany	22/29 (75.9)	3 (13.6)	18 (81.8)	-	1 (4.5)	16 (72.7)	1 (4.5)	-	6 (27.3)	2 (9.1)
Greece	84/126 (66.7)	7 (8.3)	66 (78.6)	-	3 (3.6)	34 (40.5)	-	16 (19.0)	4 (4.8)	2 (2.4)
Italy	113/131 (86.3)	11 (9.7)	103 (91.2)	-	2 (1.8)	29 (25.7)	4 (3.5)	1 (0.9)	7 (6.2)	8 (7.1)
Lithuania	22/23 (95.7)	21 (95.5)	6 (27.3)	-	-	9 (40.9)	-	-	7 (31.8)	10 (45.5)
Malta	5/5 (100.0)	5 (100.0)	-	-	-	-	-	-	-	-
Netherlands	61/69 (88.4)	43 (70.5)	15 (24.6)	-	-	16 (26.2)	13 (21.3)	-	13 (21.3)	11 (18.0)
Norway	30/35 (85.7)	17 (56.7)	22 (73.3)	-	-	11 (36.7)	1 (3.3)	1 (3.3)	14 (46.7)	15 (50.0)
Poland	50/50 (100.0)	16 (32.0)	13 (26.0)	19 (38.0)	2 (4.0)	9 (18.0)	-	-	6 (12.0)	35 (70.0)
Portugal	40/55 (72.7)	22 (55.0)	16 (40.0)	-	-	21 (52.5)	-	2 (5.0)	4 (10.0)	16 (40.0)
Spain	158/202 (78.2)	37 (23.4)	125 (79.1)	-	5 (3.2)	76 (48.1)	7 (4.4)	1 (0.6)	45 (28.5)	47 (29.7)
Sweden	34/38 (89.5)	29 (85.3)	15 (44.1)	1 (2.9)	3 (8.8)	12 (35.3)	6 (17.6)	-	5 (14.7)	12 (35.3)
United Kingdom	592/713 (83.0)	542 (91.6)	105 (17.7)	2 (0.3)	34 (5.7)	55 (9.3)	12 (2.0)	56 (9.5)	352 (59.5)	143 (24.2)
TOTAL	1746/2142 (81.5)	923 (52.9)	629 (36.0)	220 (12.6)	120 (6.9)	536 (30.7)	59 (3.4)	83 (4.8)	542 (31.0)	530 (30.4)

*Percentages of those who received S/A

Abbreviation: S/A: Sedation/Analgesia

Table S3B. Use of main analgesics, sedatives-hypnotics and neuromuscular blockers, by country, in 1496 neonates who received non invasive ventilation

Country	Neonates with S/A, n (%)	Morphine n (%)*	Fentanyl n (%)*	Sufentanil n (%)*	Ketamine n (%)*	Midazolam n (%)*	Propofol n (%)*	Chloral hydrate n (%)*	Neuromuscul ar blockers n (%)*	Acetaminoph en n (%)*
Austria	4/32(12.5)	-	-	-	-	1 (25.0)	-	3 (75.0)	-	1 (25.0)
Belgium	7/51 (13.7)	2 (28.6)	-	-	-	-	-	-	-	5 (71.4)
Cyprus	0/11 (0.0)	-	-	-	-	-	-	-	-	-
Estonia	2/4 (50.0)	-	-	-	1 (50.0)	1 (50.0)	-	-	-	1 (50.0)
Finland	26/45 (57.8)	6 (23.1)	2 (7.7)	-	1 (3.8)	-	-	-	-	24 (92.3)
France	63/225 (28.0)	1 (1.6)	-	2 (3.2)	5 (7.9)	2 (3.2)	1 (1.6)	-	-	52 (82.5)
Germany	5/17 (29.4)	2 (40.0)	1 (20.0)	-	1 (20.0)	1 (20.0)	-	-	-	2 (40.0)
Greece	6/60 (10.0)	1 (16.7)	2 (33.3)	-	-	1 (16.7)	-	4 (66.7)	-	-
Italy	26/150 (17.3)	-	21 (80.8)	-	-	4 (15.4)	1 (3.8)	-	-	3 (11.5)
Lithuania	5/21 (23.8)	4 (80.0)	-	-	-	1 (20.0)	-	-	-	-
Malta	0/5 (0.0)	-	-	-	-	-	-	-	-	-
Netherlands	6/68 (8.8)	1 (16.7)	-	-	-	1 (16.7)	-	-	-	6 (100.0)
Norway	18/94 (19.1)	4 (22.2)	1 (5.6)	-	-	-	-	-	-	16 (88.9)
Poland	19/25 (76.0)	-	1 (5.3)	-	1 (5.3)	-	-	-	-	17 (89.5)
Portugal	10/54 (18.5)	3 (30.0)	-	-	-	-	-	3 (30.0)	-	6 (60.0)
Spain	20/149 (13.4)	3 (15.0)	8 (40.0)	-	-	2 (10.0)	3 (15.0)	-	-	11 (55.0)
Sweden	8/47 (17.0)	-	2 (25.0)	-	-	-	-	-	-	6 (75.0)
United Kingdom	41/438 (9.4)	10 (24.4)	3 (7.3)	-	-	2 (4.9)	-	7 (17.1)	-	22 (53.7)
TOTAL	266/1496 (17.8)	37 (13.9)	41 (15.4)	2 (0.8)	9 (3.4)	16 (6.0)	5 (1.9)	17 (6.4)	-	172 (64.7)

*Percentages of those who received S/A

Abbreviation: S/A: Sedation/Analgesia

Table S3C. Use of main analgesics, sedatives-hypnotics and neuromuscular blockers, by country, in 3042 neonates who received spontaneous ventilation

Country	Neonates with S/A, n (%)	Morphine n (%)*	Fentanyl n (%)*	Sufentanil n (%)*	Ketamine n (%)*	Midazolam n (%)*	Propofol n (%)*	Chloral hydrate n (%)*	Neuromuscular blockers n (%)*	Acetaminophen (%)*
Austria	2/19 (10.5)	1 (50.0)	-	-	-	-	-	-	-	1 (50.0)
Belgium	6/40 (15.0)	-	1 (16.7)	-	-	-	-	1 (16.7)	-	6 (100.0)
Cyprus	0/32 (0.0)	-	-	-	-	-	-	-	-	-
Estonia	0/1 (0.0)	-	-	-	-	-	-	-	-	-
Finland	31/104 (29.8)	3 (9.7)	3 (9.7)	-	1 (3.2)	-	-	-	-	29 (93.5)
France	45/194 (23.2)	5 (11.1)	1 (2.2)	5 (11.1)	3 (6.7)	6 (13.3)	-	-	-	35 (77.8)
Germany	2/80 (2.5)	1 (50.0)	-	-	1 (50.0)	1 (50.0)	-	-	-	-
Greece	3/269 (1.1)	-	-	-	-	-	-	1 (33.3)	-	1 (33.3)
Italy	10/141 (7.1)	-	7 (70.0)	-	-	5 (50.0)	-	-	-	3 (30.0)
Lithuania	0/1 (0.0)	-	-	-	-	-	-	-	-	-
Malta	2/18 (11.1)	2 (100.0)	-	-	-	-	-	-	-	-
Netherlands	11/71 (15.5)	3 (27.3)	1 (9.1)	-	-	3 (27.3)	1 (9.1)	1 (9.1)	-	5 (45.5)
Norway	21/205 (10.2)	4 (19.0)	4 (19.0)	-	-	1 (4.8)	-	-	-	16 (76.2)
Poland	5/8 (62.5)	-	-	-	-	-	-	-	-	4 (80.0)
Portugal	12/127 (9.4)	1 (8.3)	1 (8.3)	-	1 (8.3)	1 (8.3)	-	2 (16.7)	-	9 (75.0)
Spain	20/117 (17.1)	-	5 (25.0)	-	1 (5.0)	6 (30.0)	-	-	-	8 (40.0)
Sweden	6/75 (8.0)	2 (33.3)	-	-	-	-	-	-	-	4 (66.7)
United Kingdom	106/1540 (6.9)	34 (32.1)	1 (0.9)	-	-	1 (0.9)	-	8 (7.5)	-	81 (76.4)
TOTAL	282/3042 (9.3)	56 (19.9)	24 (8.5)	5 (1.8)	7 (2.5)	24 (8.5)	1 (0.4)	13 (4.6)	-	202 (71.6)

*Percentages of those who received S/A

Abbreviation: S/A: Sedation/Analgesia

Table S4. Baseline characteristics, before and after propensity-score matching, of infants who had tracheal ventilation according to whether they received opioids and/or sedatives-hypnotics and/or general anesthetics

	Before matching				After matching			
	Opioids and/or sedatives-hypnotics and/or general anesthetics in continuous and/or bolus				Opioids and/or sedatives-hypnotics and/or general anesthetics in continuous and/or bolus			
	Yes (n=1559)	No (n=445)	Standardized differences	P value	Yes (n=427)	No (n=427)	Standardized differences	P value
Gestational age, weeks, mean(SD)	33.0 (5.4)	32.2 (4.6)	0.142	0.012	31.8 (5.0)	32.3 (4.6)	-0.098	0.139
Male sex, n (%)	933 (59.9)	247 (55.5)	0.089	0.098	244 (57.1)	239 (56.0)	0.025	0.720
Birth weight, g, mean(SD)	2003 (1058)	1823 (923)	0.172	0.002	1794 (989)	1841 (933)	-0.056	0.402
IUGR, n (%)	261 (16.4)	63 (14.2)	0.071	0.196	65 (15.2)	60 (14.1)	0.029	0.677
CRIB Score, mean(SD) †	3.6 (3.6)	2.0 (2.6)	0.523	<0.001	2.3 (2.7)	2.0 (2.7)	0.096	0.101
APGAR 1 min, mean(SD)	5.7 (2.9)	5.4 (2.8)	0.108	0.049	5.4 (2.9)	5.4 (2.8)	-0.008	0.911
APGAR 5 min, mean(SD)	7.4 (2.4)	7.4 (2.3)	0.007	0.902	7.2 (2.5)	7.4 (2.3)	-0.092	0.190
Age at admission, hours, mean (SD)	77.5 (264.6)	30.7 (183.8)	0.228	<0.001	49.5 (212.7)	31.4 (187.4)	0.097	0.103
Respiratory distress syndrome, n (%)	713 (45.7)	262 (58.9)	-0.271	<0.001	249 (58.3)	246 (57.6)	0.010	0.885
Already intubated at admission, n (%)	916 (58.8)	357 (80.2)	-0.478	<0.001	327 (76.6)	339 (79.4)	-0.068	0.325
Pain assessment, n (%)	932 (59.8)	224 (50.3)	0.190	<0.001	228 (53.4)	224 (52.5)	0.016	0.818
Duration of mechanical ventilation, hours, mean(SD)	134.2 (172.5)	38.2 (88.6)	0.699	<0.001	149.0 (183.6)	38.2 (88.5)	0.804	<0.001

† 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.

Abbreviations: SD: Standard Deviation ; IUGR: intrauterine growth retardation

Table S5. Comparison of duration of tracheal ventilation between infants who were treated with opioids and/or sedatives-hypnotics and/or general anesthetics and those who were not within each of the 5 strata created by propensity score quintiles.

Propensity quintile score (Range)	Group	No. of neonates	Duration of tracheal ventilation, hours Median (IQR)	P value*
1 (0.33 to 0.63)	Untreated	196	10.5 (5.4-24.0)	<0.001
	Treated	205	77.2 (27.5-173.1)	
2 (>0.63 to 0.76)	Untreated	114	13.0 (5.5-28.0)	<0.001
	Treated	287	88.6 (29.8-183.2)	
3 (>0.76 to 0.85)	Untreated	77	19.8 (8.0-42.5)	<0.001
	Treated	324	57.1 (18.2-122.5)	
4 (>0.85 to 0.93)	Untreated	39	19.2 (6.0-67.2)	0.001
	Treated	362	64.0 (23.6-132.9)	
5 (>0.93 to 1)	Untreated	19	7.2 (3.5-17.0)	<0.001
	Treated	381	68.5 (24.0-158.7)	
Overall	Untreated	445	12.5 (5.7-28.4)	<0.001
	Treated	1559	69.2 (23.7-151.7)	

*Mann-Whitney U test.

Abbreviation: IQ : Interquartile

Sample size calculations (extra approach)

We double checked our sample size calculation using an approach based on confidence intervals (CI) of proportions. Using NCSS-PASS 2008 (Kaysville, UT, USA), we calculated that a sample size of 2377 would produce a 95% confidence interval equal to the sample proportion plus or minus 0.20 when the estimated proportion is 0.50. We do not report proportions CI in the article because their inclusion makes tables difficult to read.