

Supplementary Online Content

Norman M, Piedvache A, Børch K, et al. Association of short antenatal corticosteroid administration-to-birth intervals with survival and morbidity among very preterm infants: results from the EPICE cohort. *JAMA Pediatr*. Published online May 15, 2017. doi:10.1001/jamapediatrics.2017.0602

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Maternity unit protocols for the first course of antenatal corticosteroids

	Number of Units	Drug used			Administration protocol		
		Betamethasone	Dexamethasone	Both	2 x 12 mg, 24 hours	2 x 12 mg, 12 hours	Other
BE:Flanders	9	7	0	2	5	2	2x8 mg, 12 h (1 unit) 2x12 mg, NA h (1 unit)
DK:Eastern	8	8	0	0	8	0	
Estonia	2	2	0	0	1	1	
FR:Northern	6	6	0	0	6	0	
FR:Burgundy	1	1	0	0	1	0	
FR:IDF*	15	12	2	0	14	1	
DE:Hesse	11	9	0	2	11	0	
DE:Saarland	2	2	0	0	1	1	
IT:Lazio	10	10	0	0	9	1	
IT:Emilia	9	9	0	0	9	0	
IT:Marche	2	2	0	0	2	0	
NL:East-Central	2	1	0	1	2	0	
PL:Wielkopolska	4	2	1	1	2	2	
PT:Northern	9	5	2	2	7	0	4x6 mg, 12 h (2 units)
PT:Lisbon	8	8	0	0	8	0	
UK:Northern	4	3	0	1	4	0	
UK:East Midlands	8	3	1	4	5	2	2x9 mg, 24 h (1 unit)
UK:Yorkshire and Humber	8	2	0	6	5	3	
SE:Stockholm	5	5	0	0	5	0	
Total	123	97 (79%)	6 (5%)	19 (15%)	105 (85%)	13 (11%)	5 (4%)

eTable 2. Characteristics of included infants and those excluded because of missing information on timing of antenatal corticosteroids (ANS)

	Study population	No information on timing of ANS	P-value	P-value adjusted on region
	n=4594	n=362		
Infant characteristics				
Gestational age, weeks [mean(sd)]	28.5 (2.2)	28.5 (2.1)	0.93#	0.42
SGA				
<3rd centile	1019 (22.2)	102 (28.3)	0.03	0.05
3-10th	465 (10.1)	35 (9.7)		
>10th	3109 (67.7)	223 (61.9)		
Sex				
Male	2496 (54.3)	197 (54.6)	0.93	0.76
Female	2097 (45.7)	164 (45.4)		
Surfactant <2h after birth				
No	2510 (56.7)	162 (56.5)	0.93	0.38
Yes	1915 (43.3)	125 (43.6)		
Maternal characteristics				
Age, yrs [mean(sd)]	30.0 (6.2)	30.0 (6.3)	0.95#	0.49
Parity				
Primiparous	2469 (54.2)	172 (49.9)	0.12	0.13
Multiparous	2085 (45.8)	173 (50.1)		
Preeclampsia, eclampsia, HELLP				
No	3642 (80.3)	213 (75)	0.03	<0.001
Yes	894 (19.7)	71 (25)		
Preterm prelabor rupture of membranes				
No	3357 (74)	193 (67.7)	0.02	0.16
Yes	1182 (26)	92 (32.3)		
Delivery onset				
Spontaneous/induced	2501 (55)	176 (51)	0.15	0.02
Cesarean	2045 (45)	169 (49)		
Mode of delivery				
Vaginal	1634 (35.9)	92 (25.9)	<0.001	0.01
Cesarean	2919 (64.1)	263 (74.1)		
Delivery at level III unit				
No	1106 (24.1)	105 (29)	0.04	0.01
Yes	3483 (75.9)	257 (71)		
Delivery on day of admission				
No	1089 (24.6)	57 (24.3)	0.78	0.47
Yes	3335 (75.4)	178 (75.7)		

Region				
BE:Flanders	429 (9.3)	8 (2.2)	<0.001	
DK:Eastern	182 (4)	12 (3.3)		
Estonia	112 (2.4)	1 (0.3)		
FR:Northern	169 (3.7)	1 (0.3)		
FR:Burgundy	56 (1.2)	1 (0.3)		
FR:IDF	543 (11.8)	17 (4.7)		
DE:Hesse	233 (5.1)	103 (28.5)		
DE:Saarland	55 (1.2)	26 (7.2)		
IT:Lazio	314 (6.8)	17 (4.7)		
IT:Emilia	263 (5.7)	11 (3)		
IT:Marche	76 (1.7)	0 (0)		
NL:East-Central	240 (5.2)	7 (1.9)		
PL:Wielkopolska	194 (4.2)	5 (1.4)		
PT:Northern	187 (4.1)	3 (0.8)		
PT:Lisbon	291 (6.3)	3 (0.8)		
UK:Northern	238 (5.2)	52 (14.4)		
UK:East Midlands	384 (8.4)	17 (4.7)		
UK:Yorkshire & Humber	457 (10)	77 (21.3)		
SE:Stockholm	171 (3.7)	1 (0.3)		

Data are numbers (%) if not stated otherwise.

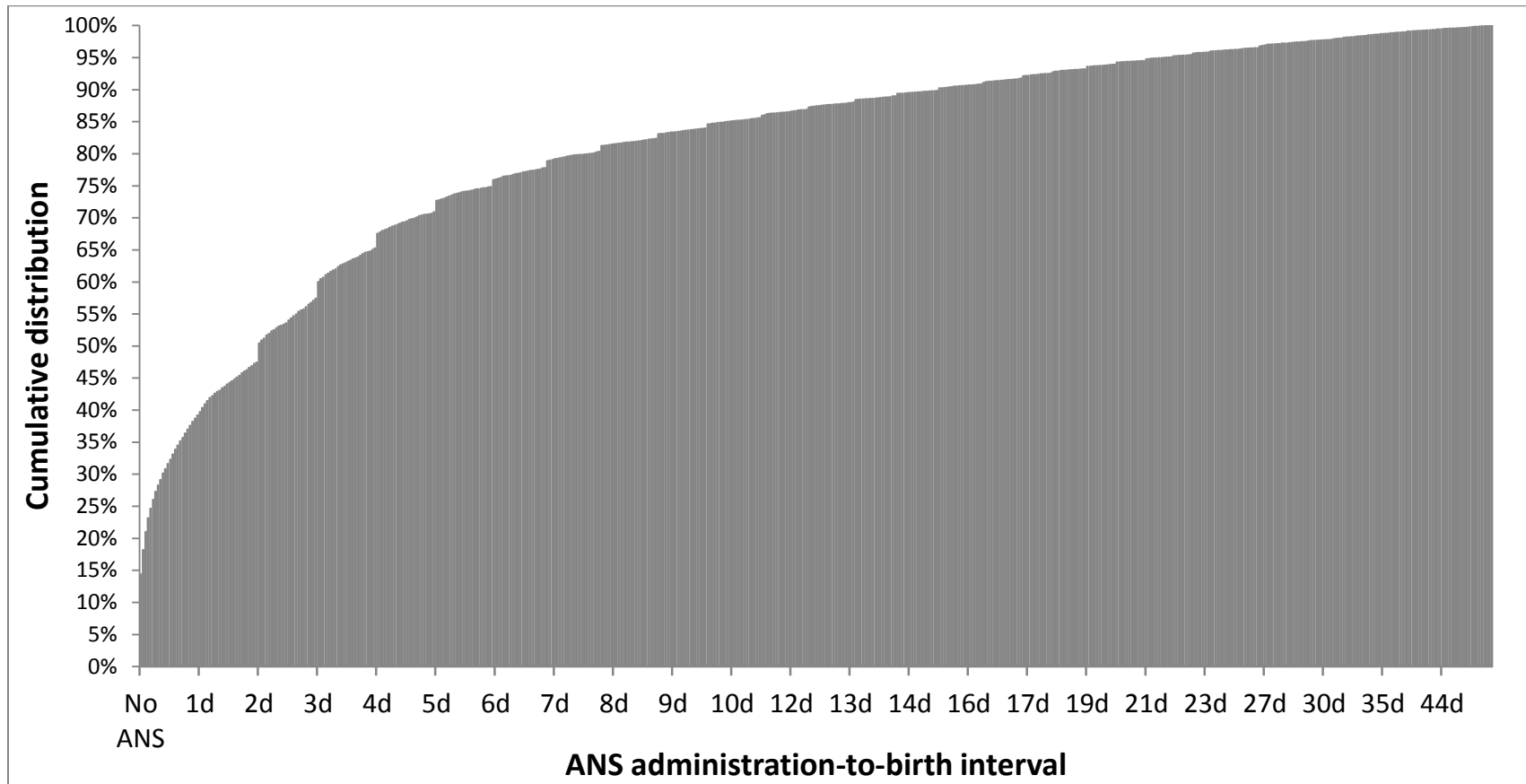
Kruskal-Wallis test.

eTable 3. Simulation of in-hospital mortality if providing ANS hours before delivery to infants who did not receive ANS (n = 661)

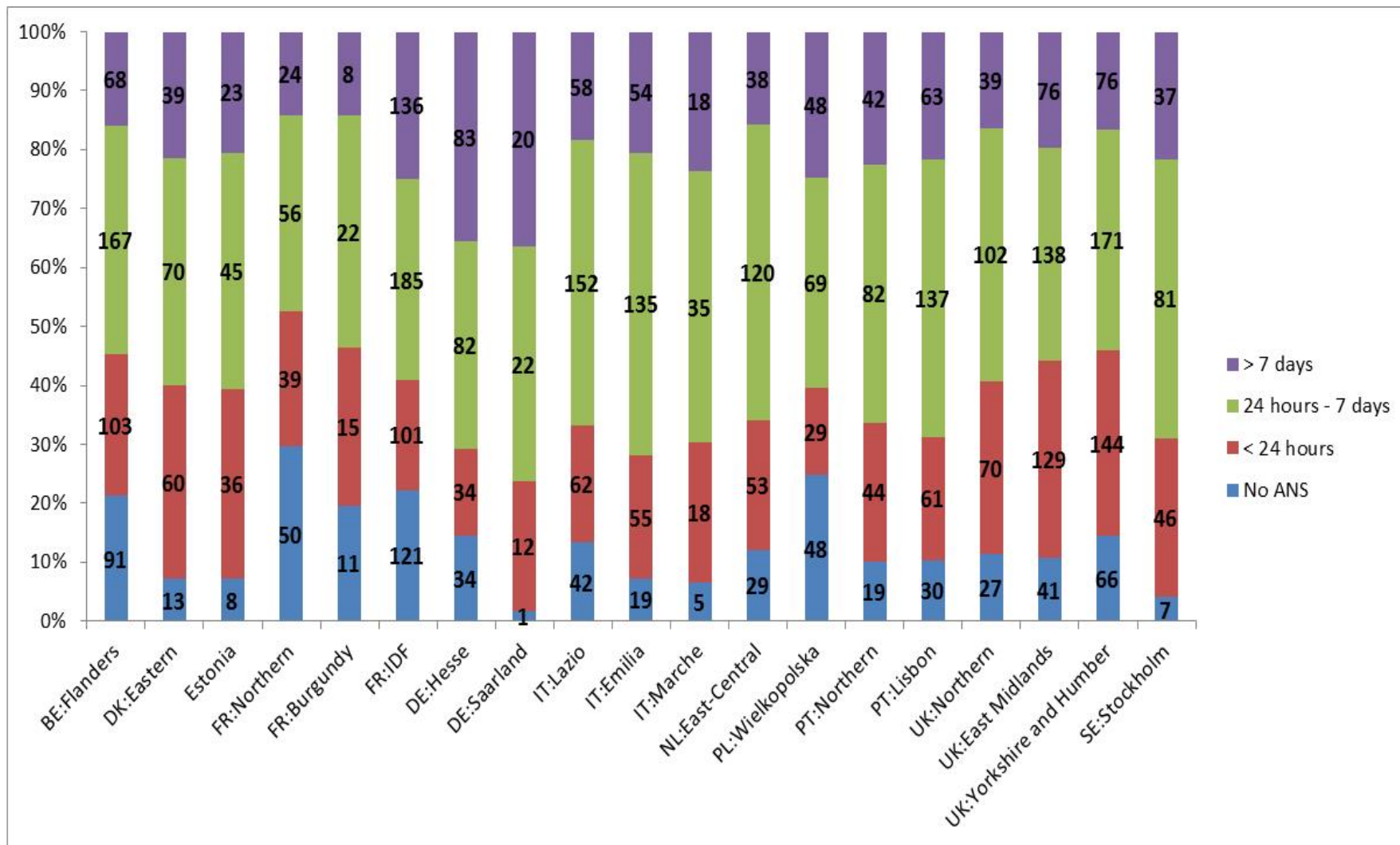
Simulations	In-hospital mortality	In-hospital mortality or severe neonatal morbidity¹
No ANS (observed situation)		
Observed events (n)	114	177
Predicted events (n)	114	177
If ANS <3hrs		
Predicted events (n)	84	139
Reduction in events (n)	30	38
% reduction	26%	21%
If ANS 3-5 hours		
Predicted events (n)	72	134
Reduction in events (n)	42	43
% reduction	37%	24%
If ANS 6-12 hours		
Predicted events (n)	56	132
Reduction in events (n)	58	45
% reduction	51%	25%

NOTES: ¹severe neonatal morbidity includes: intraventricular hemorrhage (IVH) grade ≥ 3 , cystic periventricular leukomalacia (cPVL), surgical necrotizing enterocolitis or retinopathy of prematurity stage ≥ 3

eFigure 1. Cumulative distribution of administration-to-birth intervals of antenatal corticosteroids (ANS) for very preterm birth (delivered livebirths only)



eFigure 2. Administration of antenatal corticosteroids and administration-to-birth intervals (colored) by European region



eFigure 3. Association between timing of antenatal corticosteroids (ANS) and a composite of in-hospital mortality or severe neonatal morbidity

