ANTENATAL STEROIDS FOR PRETERM BIRTH: OPTIMIZING USE AS A NEW QUALITY INDICATOR

Jesper Padkær Petersen, Charlotte Brix Andersson, Ulrik Schiøler Kesmodel, Lene Friis Eskildsen, Pernille Fjordside Iversen, Heidi Cueto. ANTENATAL STEROIDS FOR PRETERM BIRTH: OPTIMIZING USE AS A POSSIBLE NEW QUALITY INDICATOR

Jesper Padkær Petersen, Charlotte Brix Andersson, Ulrik Schiøler Kesmodel, Lene Friis Eskildsen, Pernille Fjordside Iversen, Heidi Cueto.

- Antenatal steroids (ANS) are vital for reducing morbidity and mortality in preterm infants.
- Randomized controlled trials (RCTs) support efficacy.
- Observational data raise concerns about neurocognitive development in fetuses exposed to ANS but not born preterm.
- RCTs in the developing world also highlight the need to optimize ANS use.
- Most quality registers focus on preterm children, overlooking those born later.

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**Cochrane** Database of Systematic Reviews

Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth (Review)

McGoldrick E, Stewart F, Parker R, Dalziel SR

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#### Neonatal/child outcomes

Antenatal corticosteroids reduce the risk of:

- **perinatal death** (risk ratio (RR) 0.85, 95% confidence interval (CI) 0.77 to 0.93; 9833 infants; 14 studies; high-certainty evidence; 2.3% fewer, 95% CI 1.1% to 3.6% fewer),
- neonatal death (RR 0.78, 95% CI 0.70 to 0.87; 10,609 infants; 22 studies; high-certainty evidence; 2.6% fewer, 95% CI 1.5% to 3.6% fewer),
- **respiratory distress syndrome** (RR 0.71, 95% CI 0.65 to 0.78; 11,183 infants; studies = 26; high-certainty evidence; 4.3% fewer, 95% CI 3.2% to 5.2% fewer).

Antenatal corticosteroids probably reduce the risk of IVH (RR 0.58, 95% CI 0.45 to 0.75; 8475 infants; 12 studies; moderate-certainty evidence; 1.4% fewer, 95% CI 0.8% to 1.8% fewer), and probably have little to no effect on birthweight (mean difference (MD) -14.02 g, 95% CI -33.79 to 5.76; 9551 infants; 19 studies; high-certainty evidence).

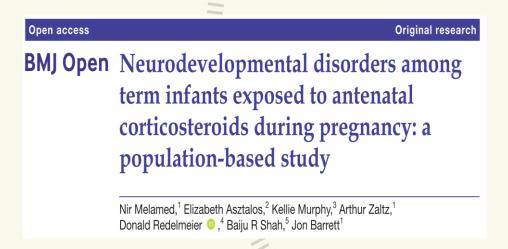
Antenatal corticosteroids probably lead to a reduction in developmental delay in childhood (RR 0.51, 95% CI 0.27 to 0.97; 600 children; 3 studies; moderate-certainty evidence; 3.8% fewer, 95% CI 0.2% to 5.7% fewer).

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May 19, 2020

Associations Between Maternal Antenatal Corticosteroid Treatment and Mental and Behavioral Disorders in Children

Katri Räikkönen, PhD<sup>1</sup>; Mika Gissler, DrPhil<sup>2,3,4</sup>; Eero Kajantie, MD, DMSc<sup>5,6,7,8</sup>

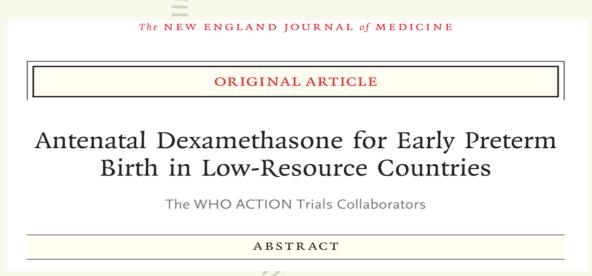


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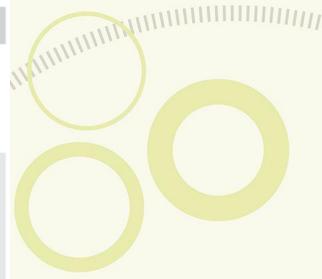
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TABLE 2 Perinatal interventions in very preterm live births (GA <32 weeks; survivors and in-hospital deaths).

	Any antenatal steroids <28 weeks GA n (%) <sup>a</sup>	Any antenatal steroids 28- 31 weeks GA n (%) <sup>a</sup>	C-section, <28 wks GA n (%) <sup>a</sup>	C-section, 28–31 weeks GA n (%) <sup>a</sup>
Denmark	No data	No data	90 (51% [43-58])	233 (70% [64-74])
D1-Capital Region	No data	No data	48/82 (59)	93/125 (74)
D2-East Region				28/39 (72)
D3-South Region			15/30 (50)	44/56 (79)
D4-Mid Region			19/43 (44)	42/73 (58)
D5-North Region			8/22 (36)	26/42 (62)
Finland	107 (95% [89-98])b	205 (95% [92-98]) <sup>b</sup>	56 (58% [47-68])	159 (68% [62-74])
F1-South Region (Helsinki)	45 (94)	78 (95)	20 (50)	70 (72)
F2-East Region (Kuopio)	12 (100)	22 (92)	2 (25)	23 (77)
F3-North Region (Oulu)	16 (89)	32 (94)	14 (70)	16 (59)
F4-Central Region (Tampere)	17 (94)	27 (96)	9 (82)	22 (62)
F5-West Region (Turku)	17 (100)	46 (98)	11 (61)	28 (64)
Iceland	12 (86% [57-98])	31 (100% [89-100])	4 (29% [8.4-58])	15 (48% [30-67])
I1-Iceland	12 (86)	31 (100)	4 (29)	15 (48)
Norway	163 (96% [92-99])	288 (91% [87-94])	92 (53% [45-60])	192 (60% [54-65])
N1-Southeast Region	110 (95)	165 (95)	65 (57)	114 (65)
N2-West Region	26 (87)	58 (84)	13 (43)	28 (41)
N3-Mid Region	20 (100)	39 (89)	11 (52)	27 (61)
N4-North Region	7 (88)	26 (84)	3 (38)	23 (74)
Sweden	286 (93% [90-96])	530 (91% [88-93])	186 (57% [52-63])	452 (70% [66-73])
S1-North Region	27 (97)	30 (81)	17 (61)	28 (68)
S2-Mid Region	38 (81) <sup>c</sup>	109 (87)	28 (49)	105 (76)
S3-East Region	83 (97)	138 (96)	54 (62)	104 (68)
S4-West Region	48 (96)	112 (94)	35 (67)	89 (71)
S5-Southeast Region	30 (97)	49 (89)	19 (53)	45 (65)
S6-South Region	60 (92)	92 (88)	33 (51)	81 (68)
Nordic countries, total	568 (94% [92-96])	1054 (92% [90-93])	428 (54% [51-58])	1051 (67% [65-69])

<sup>&</sup>lt;sup>a</sup>95% confidence intervals for proportions are presented for countries.

Norman M, Padkær Petersen J, Stensvold HJ, Thorkelsson T, Helenius K, Brix Andersson C, et al. Preterm birth in the Nordic countries—Capacity, management and outcome in neonatal care. *Acta Paediatr*. 2023; 112: 1422–1433. https://doi.org/10.1111/apa.16753



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Sweden	204 (029)	[00 04])	520 /018/	/1co 001	114 (65)
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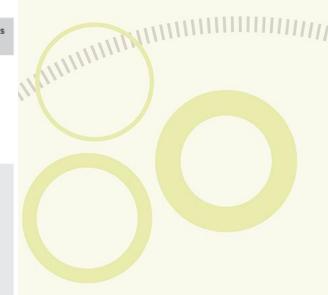
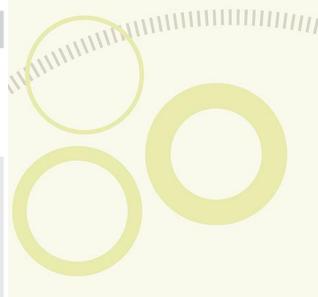


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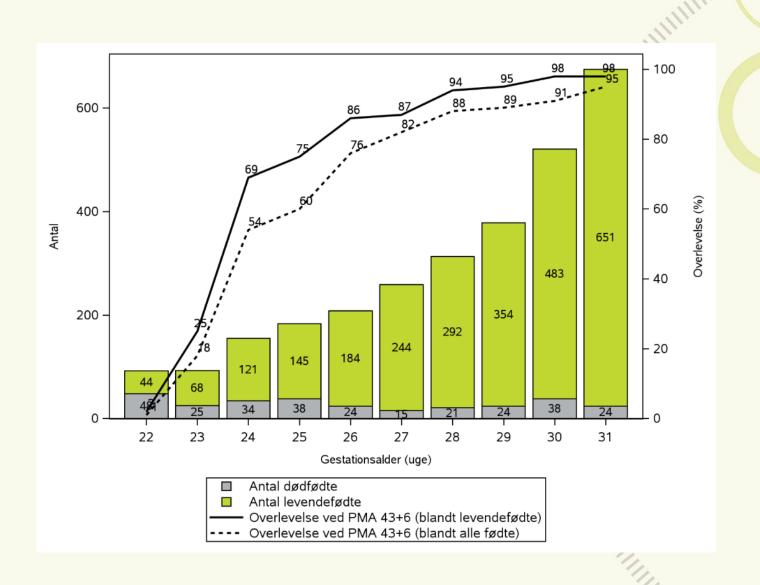
	Any antena <28 weeks	tal steroids GA n (%)*	Any antena 31 weeks G	tal steroids 28- A n (%)*	C)-74
Denmark	No data		No data		
D1-Capital Region	No data		No data		4-74
D2-East Region					
D3-South Region					1
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	S6-South Region  Nordic countries, total	50 (97) 60 (92) 568 (94% [92-96])	92 (88) 1054 (92% [90–93])	33 (51) 428 (54% [51–58])	81 (68) 1051 (67% [65-69]

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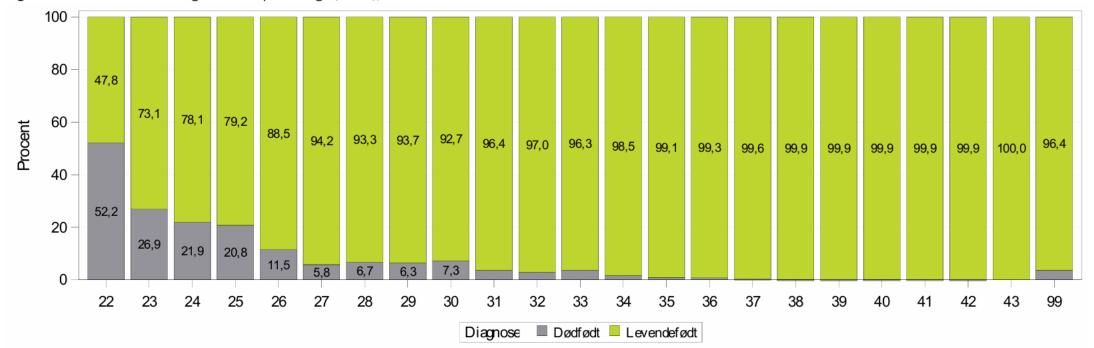


	Tabel 7. Antal	levendefødte og	g dødfødte i	per GA uge	(22-43), 2019-2023
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	GA22	GA23	GA24	GA25	GA26	GA27	GA28	GA29	GA30	GA31	GA32	GA33	GA34	GA35	GA36	GA37	GA38	GA39	GA40	GA41	GA42	GA43	GA99	I alt
Dødfødt	48	25	34	38	24	15	21	24	38	24	29	55	39	32	53	64	58	69	75	44	6	0	#	816
Levendefødt	44	68	121	145	184	244	292	354	483	651	944	1.418	2.506	3.527	7.198	16.938	38.968	65.225	85.175	68.393	6.125	15	27	299.045
Pop. i alt	92	93	155	183	208	259	313	378	521	675	973	1.473	2.545	3.559	7.251	17.002	39.026	65.294	85.250	68.437	6.131	15	28	299.861
Procent pop.	0,03%	0,03%	0,05%	0,06%	0,07%	0,09%	0,10%	0,13%	0,17%	0,23%	0,32%	0,49%	0,85%	1,19%	2,42%	5,67%	13,0%	21,8%	28,4%	22,8%	2,04%	0,01%	0,01%	

GA99= Ukendt GA

Figur 5. Andel levendefødte og dødfødte per GA uge (22-43), 2019-2023

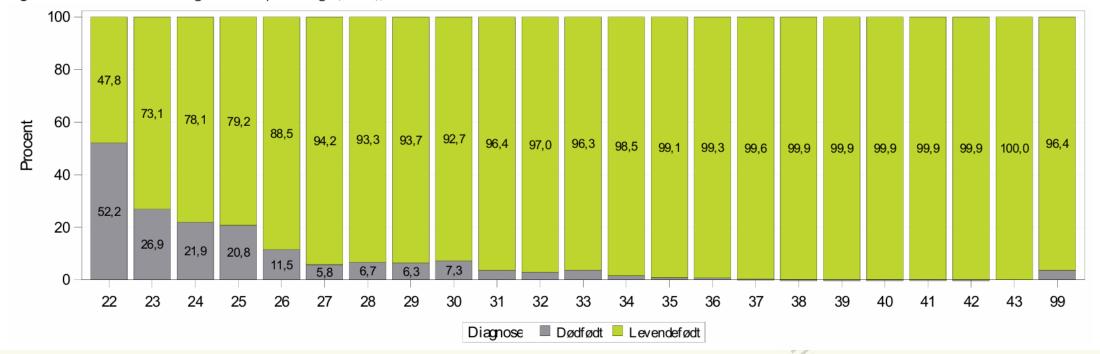


	GA22	GA23	GA24	GA25	GA26	GA27	GA28	GA29	GA30	GA31	GA32	GA33	GA34	GA35	GA36	GA37	GA38	GA39	GA40	GA41	GA42	GA43	GA99	I alt
Dødfødt	48	25	34	38	24	15	21	24	38	24	29	55	39	32	53	64	58	69	75	44	6	0	#	816
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Procent pop.	0,03%	0,03%	0,05%	0,06%	0,07%	0,09%	0,10%	0,13%	0,17%	0,23%	0,32%	0,49%	0,85%	1,19%	2,42%	5,67%	13,0%	21,8%	28,4%	22,8%	2,04%	0,01%	0,01%	

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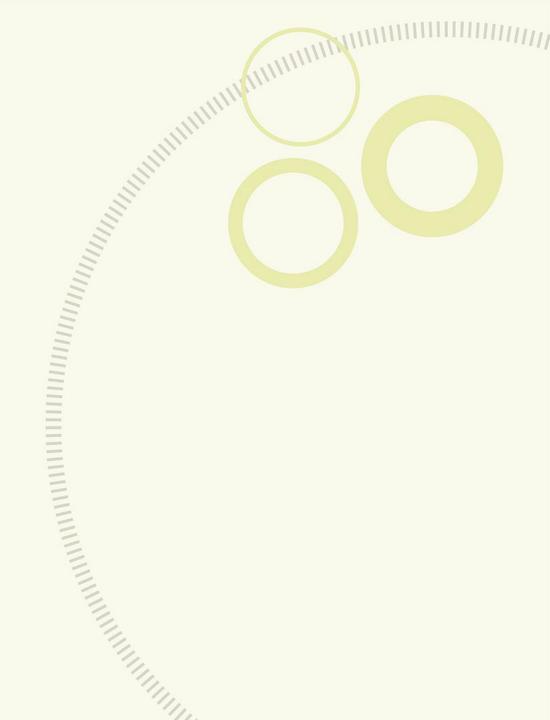
Figur 5. Andel levendefødte og dødfødte per GA uge (22-43), 2019-2023



THURING THURING THE PARTY OF TH Tabel 7. Antal levendefødte og dødfødte per GA uge (22-43), 2019-2023 GA42 GA43 GA99 I alt **Tabel 7.** Antal levendefødte og dødfødte per GA uge (22-43), 2019-2023 0 816 # **GA22** GA23 GA24 GA25 GA26 GA27 GA28 **GA29 GA30** GA31 GA32 GA33 13 6.125 15 27 299.045 6.131 299.861 15 28 Dødfødt 29 25 34 38 24 15 21 24 55 48 24 38 2,04% 0,01% 0,01% Levendefødt 44 68 121 145 184 244 292 354 483 651 944 1.418 Pop. i alt 92 93 155 183 208 259 313 378 521 675 973 1.473 0,07% 0,17% 0,49% Procent pop. 0,03% 0,03% 0,05% 0,06% 0,09% 0,10% 0,13% 0,23% 0,32% GA99= Ukendt GA 73,1 78.1 60 79,2 **Procent** 88,5 93,3 93,7 92,7 96.4 96,3 97,0 96,4 98.5 99.1 99,3 99.6 99,9 99.9 99.9 100,0 40 52,2 20 26.9 21,9 20,8 11,5 6,7 7,3 5.8 6,3 22 23 24 25 26 28 29 30 32 33 34 35 36 37 38 39 40 41 42 43 99 ■ Dødfødt ■ Levendefødt

Diagnose

A 1000 births < GA 34 pr year (approximately)

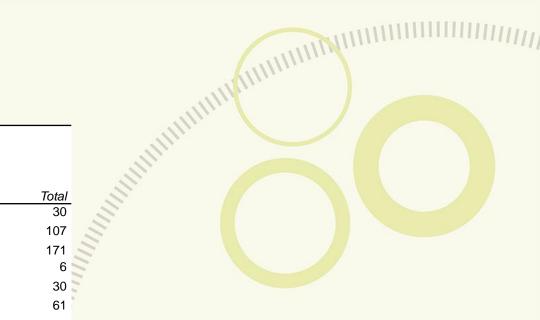


#### Methods

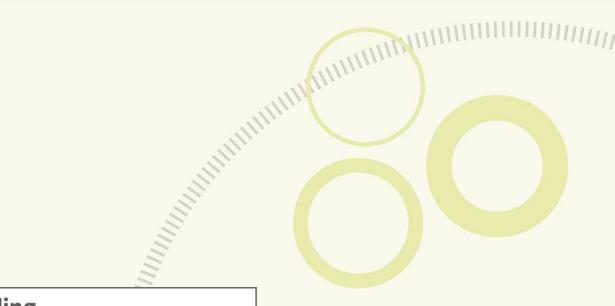
- We performed a cross-sectional study, analyzing aggregated rate data from all 56,339 births
   Denmark 2023.
- The National Hospital Medication Register (NHMR) provided data on ANS use.
- NHMR registrations were compared with ANS codes from the Danish National Patient Register.
- Gestational age (GA) at administration and at birth was obtained from the Danish National Clinical Quality Database for Births.

- NHMR identified 1,309 births with ANS use. ANS administration occurred in 81.2% of all 867 births with GA <34 weeks.</li>
- o First administration was given at GA<34 weeks in 99.8% of the cases and 64.2% before 32 weeks.
- Among all birth with ANS administered at GA<32 weeks,</li>
  - o 57.6% resulted in births at GA <34 weeks.
  - 16.0% at GA 34-36 weeks.
  - o 26.4% at 37+ weeks.
- Among births with ANS administered at GA 32-33 weeks,
  - 48.4% resulted in births at GA <34 weeks,</li>
  - o 19.8% at GA 34-36 weeks
  - o 24.0% at 37+ weeks.
- Rates varied across hospitals.

Table o	of hospital by s	teroid_profyla	kse	
hospital		steroid_pro	ofylakse	
Frequency				
	Kun SMR	Kun LPR	Begge	Total
Aabenraa	30	0	0	30
Aalborg	107	0	0	107
Aarhus	164	0	7	171
Bornholm	6	0	0	6
Esbjerg	15	2	13	30
Gødstrup	61	0	0	61
Herlev	102	1	1	104
Hillerød	68	0	6	74
Holbæk	33	0	0	33
Horsens	13	0	2	15
Hvidovre	10	5	103	118
Kolding	57	0	0	57
Nykøbing F.	4	0	1	5
Odense/Svendborg	110	0	1	111
Randers	50	0	0	50
Rigshospitalet	174	1	6	181
Roskilde	10	1	17	28
Slagelse	63	0	1	64
Thisted	3	0	0	3
Vendsyssel	30	0	0	30
Viborg	9	2	32	43
Total	1119	12	190	1321







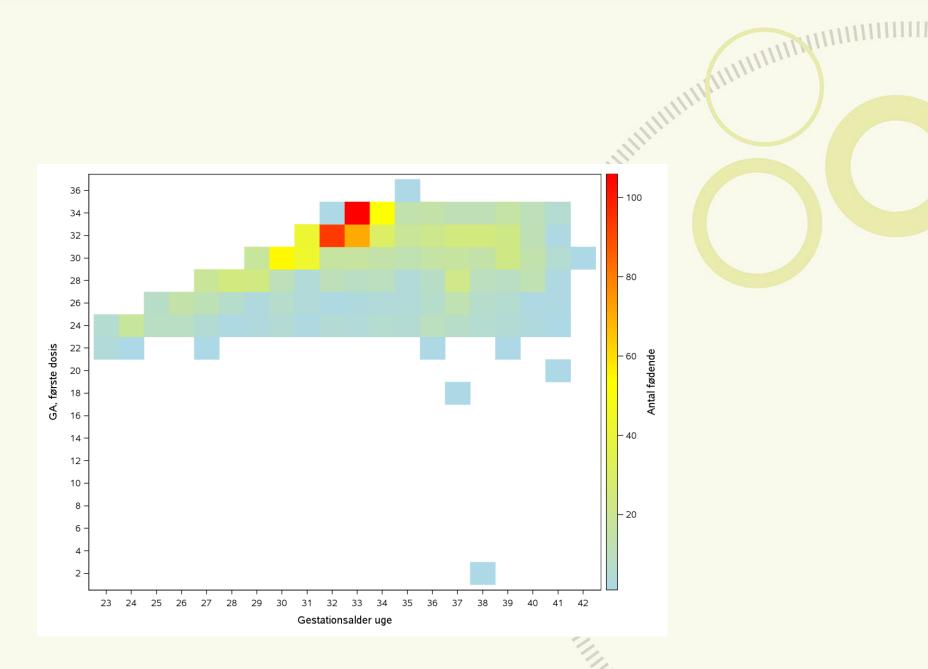
Andel af fødselspop., som har fået mindst én steroidbehandling i graviditeten, per GA-gruppe. Beregnet for hhv. alle singletonfødsler og singletonfødsler af levendefødt barn.

GA (fødsel)	N	Levendefødte	Dødfødte	Steroid	oeh. (alle)	Steroidbeh. (	levendefødte)
				Ja	Nej	Ja	Nej
GA 22-27	137	105	32	88 (64,2%)	49 (35,8%)	87 (82,9%)	18 (17,1%)
GA 28-31	257	244	13	220 (85,6%)	37 (14,4%)	218 (89,3%)	26 (10,7%)
GA 32-33	347	338	9	289 (83,3%)	58 (16,7%)	288 (85,2%)	50 (14,8%)
GA 34+	54.716	54.627	89	521 (1,0%)	54.195 (99,0%)	520 (1,0%)	54.107 (99,0%)
Total	55.457	55.314	143	1.118	54.339	1.113	54.201

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Table	of b_sor_ho	spital by ga_grup	рре		
b_sor_hospital(Hospitalsnavn til			-		
afrapportering SOR)		ga_grupp	e(GA, fødsel)		
Frequency		0 0	,		
	Ukendt	GA 24+0 -	GA 34+0 -	GA	
	GA	33+6	36+6	37+0 -	Total
Aabenraa	0	17	5	8	30
Aalborg	0	54	26	27	107
Aarhus	3	113	27	28	171
Bornholm	0	0	1	5	6
Esbjerg	0	19	5	4	28
Gødstrup	0	30	17	14	61
Herlev	0	45	22	36	103
Hillerød	0	35	15	24	74
Holbæk	0	15	8	10	33
Horsens	0	1	1	13	15
Hvidovre	0	52	30	31	113
Kolding	1	29	15	12	57
Nykøbing F.	0	0	2	3	5
Odense/Svendborg	2	69	12	28	111
Randers	0	22	14	14	50
Rigshospitalet	5	123	25	27	180
Roskilde	0	13	7	7	27
Slagelse	0	30	17	17	64
Thisted	0	2	0	1	3
Vendsyssel	0	9	5	16	30
Viborg	0	20	5	16	41
Total	11	698	259	341	1309

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		of first_ac	dm_dato_ga by	ga_gruppe		
first_adm_dato_ga(0 første dosis)	JA,		as arun	pe(GA, fødsel	1	
Frequency		Ukendt	ga_grup; GA 24+0 -	GA 34+0 -	) GA	
roquonoy		GA	33+6	36+6	37+0 -	Total
		1	0	0	0	1
	2	0	0	0	1	1
	18	0	0	0	1	1
	20	0	0	0	1	1
	21	0	0	1	0	1
	22	4	2	0	1	7
	23	6	25	8	5	44
	24	0	40	14	19	73
	25	0	24	4	15	43
	26	0	39	12	17	68
	27	0	49	11	23	83
	28	0	55	11	35	101
	29	0	68	15	36	119
	30	0	82	29	41	152
	31	0	89	29	27	145
	32	0	118	42	62	222
	33	0	107	79	57	243
	34 35	0 0	0	3 1	0	3 1
Total	JJ	11	698	259	341	1309



Viden til et bedre sundhedsvæsen www.rkkp.dk

#### Conclusions

- Approximately one out of four children exposed to ANS, was not born preterm, and a substantial fraction of those born at GA <34 weeks did not receive ANS treatment. These findings suggest that ANS utilization could be further optimized in Denmark and other locations.
- NHMR appears a feasible source of information on ANS use in Denmark.

