Practice patterns in the administration of late preterm antenatal corticosteroids

Moti Gulersen, MD, MSc; Cynthia Gyamfi-Bannerman, MD, MSc; Michelle Greenman, MD; Erez Lenchner, PhD; Burton Rochelson, MD; Eran Bornstein, MD

BACKGROUND: Given the unpredictable nature of preterm birth and the short-term impact of antenatal corticosteroids on neonatal outcomes, optimal timing of antenatal corticosteroid administration (2–7 days from expected birth) remains challenging.

OBJECTIVE: We set out to evaluate the likelihood of delivery between 2 and 7 days after antenatal corticosteroid administration in the late preterm period and whether this differs based on the indication for corticosteroid administration.

STUDY DESIGN: Retrospective cohort of all singletons that received antenatal corticosteroids in the late preterm period (34 0/7 to 36 6/7 weeks' gestation) and delivered within a large health system between November 2017 and March 2020. Women who received antenatal corticosteroids before the late preterm period, major fetal structural malformations, and cases with missing data were excluded. Cases were stratified on the basis of the indication for antenatal corticosteroid administration, that is, anticipated spontaneous late preterm birth or medically indicated late preterm birth. The primary outcome was delivery between 2 and 7 days after the administration of the first dose of antenatal corticosteroids. Secondary outcomes included time interval from antenatal corticosteroid administration to delivery and delivery during the first 2 days or later than 7 days after antenatal corticosteroid administration. Multivariable logistic regression was performed to evaluate factors associated with optimal timing while adjusting for potential confounders.

RESULTS: Of the 1238 patients included in the study, 656 (53%) delivered within the first day after antenatal corticosteroid administration and thus received only the first of 2 doses. Regardless of the indication for late preterm antenatal corticosteroid administration, the likelihood of delivery between 2 and 7 days later was 13.3% (165 of 1238). Moreover, it was more common (23.4% vs 5.0%; $P \leq .001$) (Table 2) and more likely (adjusted odds ratio, 5.88; 95% confidence interval, 4.00–9.09) in women at risk of medically indicated preterm birth than in those with anticipated spontaneous preterm birth. Furthermore, women with anticipated spontaneous preterm birth had a shorter time interval from antenatal corticosteroid administration to delivery (10.7 vs 49.71 hour; $P \leq .001$).

CONCLUSION: Regardless of the indication for late preterm antenatal corticosteroid administration, the likelihood of delivery between 2 and 7 days later was low. Nevertheless, our data suggested that delivery within the desired time interval of antenatal corticosteroid administration is more common in women at risk of medically indicated late preterm birth compared with those at risk of spontaneous late preterm birth.

Key words: betamethasone, corticosteroids, late preterm birth, medically indicated preterm birth, optimal timing, preterm birth, spontaneous preterm birth, time interval

Introduction

Late preterm birth, defined as birth between 34 0/7 and 36 6/7 weeks' gestation, accounts for more than 70% of all preterm births in the United States.[1–3] Although most late preterm newborns seem well at birth, have short hospital stays, and favorable long-term outcomes, they are at increased risk of morbidity and mortality compared with their term counterparts.[4–11] With the recent reported rise in preterm birth rate largely reflective of the increase in late preterm births in the United States,[1,2] and the known associated risk for adverse outcomes in this cohort,[4–11] management strategies have been investigated for women at risk of late preterm birth to reduce the likelihood of such adverse outcomes.[12–14]

Antenatal corticosteroid (ACS) administration for pregnant women at risk of early preterm birth (24 0/7 to 33 6/7 weeks' gestation) represents one

From the Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, North Shore University Hospital, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY (Drs Gulersen, Greenman, and Rochelson); Department of Obstetrics, Gynecology, and Reproductive Sciences University of California, San Diego La Jolla, CA (Dr Gyamfi-Bannerman); Biostatistics and Data Management, New York University Rory Meyers College of Nursing, New York, NY (Dr Lenchner); Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Lenox Hill Hospital, Zucker School of Medicine at Hofstra/Northwell, New York, NY (Dr Bornstein)

C.G.B. disclosed that she receives funding by an unrestricted grant from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Heart, Lung, and Blood Institute. The remaining authors report no conflict of interest.

This study was presented as a poster (final abstract number 881) at the 41st Annual Meeting of the Society for Maternal-Fetal Medicine, held virtually, January 25–30, 2021.

Cite this article as: Gulersen M, Gyamfi-Bannerman C, Greenman M, et al. Practice patterns in the administration of late preterm antenatal corticosteroids. Am J Obstet Gynecol Glob Rep 2021;1:100014.

Corresponding author: Moti Gulersen, MD, MSc. mgulersen1@northwell.edu

2666-5778/$36.00

http://dx.doi.org/10.1016/j.xagr.2021.100014

AJOG Global Reports at a Glance

Why was this study conducted?

Data from neonates born in the early preterm period suggested that the administration of antenatal corticosteroids (ACSs) between 2 and 7 days before delivery is optimal. We set out to evaluate the likelihood of delivery between 2 and 7 days after late preterm ACS administration and whether this differs based on the indication for corticosteroid administration.

Key findings

Regardless of the indication for late preterm ACS administration, the likelihood of delivery between 2 and 7 days later was low, as only 13.3% of our study cohort delivered between that time interval. Delivery between 2 and 7 days after late preterm ACS administration was more likely in women at risk of medically indicated late preterm birth than in women at risk of spontaneous late preterm birth.

What does this add to what is known?

Current practice patterns of late preterm ACSs have suggested that delivery between the desired times of administration (2−7 days) is more common in women at risk of medically indicated preterm birth compared with those at risk of spontaneous preterm birth.

of the most important antenatal therapies available to improve neonatal outcomes.[15,16] When timed appropriately (delivery between 2 to 7 days after administration), antenatal cortiocsteroids (ACS) have been associated with a significant reduction in neonatal morbidity and mortality in several randomized clinical trials.[16−23] A lack of supportive data and the underappreciated risks associated with late preterm infants had initially limited the recommendation of corticosteroid use to extend to women at risk of late preterm delivery.[18,24] However, in a recent multicenter, randomized, double-blind, placebo-controlled trial, ACS administration (intended as 12 mg of betamethasone given 24 hours apart) was associated with a decrease in neonatal respiratory morbidities in singleton pregnancies at risk of late preterm birth.[14] These benefits were found despite the challenges in predicting the timing of delivery, which resulted in only 60% of the study participants receiving the full course of ACSs.[14]

Given the unpredictable nature of preterm birth and the short-term impact of ACSs on neonatal outcomes, optimal timing of ACS administration remains challenging.[25−27] We set out to evaluate the likelihood of delivery between 2 and 7 days after ACS administration in the late preterm period and whether this differs based on indication for corticosteroid administration.

Materials and Methods

This was a retrospective cohort study of all women with singleton pregnancies who were prescribed ACSs in the late preterm period (34 0/7 to 36 6/7 weeks' gestation) and delivered within a multicenter health system between November 2017 and March 2020. Before the study period, our institutional guidelines suggested consideration for the administration of ACSs, defined as 2 doses of betamethasone 12 mg given intramuscularly 24 hours apart, in women with a singleton pregnancy in the late preterm period who were at high risk of preterm birth within the next 7 days. In addition, these guidelines suggested that ACSs be avoided in women with chorioamnionitis or pregestational diabetes mellitus and those who received corticosteroids before the late preterm period in the same pregnancy and that tocolysis should not be used to allow for corticosteroid administration. The decision to administer ACSs was left to the discretion of the obstetrician, with maternal-fetal medicine consultation available as needed.

All women with singleton pregnancies who were prescribed ACSs during the late preterm period and received at least 1 of 2 doses were included. The exclusion criteria included the administration of ACSs before the late preterm period in the same pregnancy, major fetal structural malformations, and cases with missing data regarding the indication for ACS administration. Maternal characteristics, such as age, body mass index (BMI), race and ethnicity, and parity, were collected. In addition, a detailed review of each medical record was performed to obtain data regarding the presence or absence of pregnancy-related complications and/or risk factors for preterm birth and the indication for ACS administration.

Cases were stratified into 2 groups based on the indication for ACS administration: either anticipated spontaneous late preterm birth (ie, preterm labor with intact membranes based on evaluation by the managing obstetrician, which was suspected to result in preterm birth within the next 7 days, or preterm prelabor rupture of membranes) or medically indicated late preterm birth (ie, hypertensive disorders of pregnancy, fetal growth restriction, oligohydramnios, intrahepatic cholestasis of pregnancy, nonreassuring fetal status, placental abruption, placenta previa, placenta accreta, vasa previa, or other [ie, history of classical cesarean delivery or uterine rupture, poor maternal or obstetrical history, alloimmunization]). The primary outcome was delivery between 2 and 7 days after the first dose of betamethasone administration. We considered 2 to 7 days as an optimal time interval, extrapolated from data on the use of ACSs in women with preterm birth at <34 weeks' gestation,[28] as corticosteroid administration is dosed on a 48-hour schedule, and neonatal benefit may diminish with a latency period of >7 days.[29−32] Secondary outcomes included time interval from ACS administration to delivery, delivery before 2 days or later than 7 days after ACS administration, gestational age at delivery and delivery at <37 weeks'

gestation. Demographic data, baseline characteristics, and outcome data were compared between the 2 groups using chi-square and Wilcoxon rank-sum testing with statistical significance set at $P<.05$. In addition, multivariable logistic regression was performed to evaluate factors associated with optimal timing of ACS administration while adjusting for potential confounders, such as maternal age, race and ethnicity, BMI, parity, gestational age at ACS administration, gestational diabetes mellitus, and history of preterm birth. Data were presented as adjusted odds ratios (aORs) with 95% confidence intervals (95% CIs). An institutional review board approval was obtained.

Results

During the study period, there were approximately 45,060 deliveries that took place at the study centers. Our study included a total of 1272 (2.8%) women with singleton gestations who were prescribed ACSs during the late preterm period and received at least 1 of 2 doses of betamethasone. Women who received ACSs before the late preterm period in the same pregnancy (5), cases with major fetal structural malformations (3), and cases with missing data regarding the indication for ACS administration (26) were excluded. After applying our exclusion criteria, 1238 patients composed the study cohort and were further analyzed. Of those patients, 679 (54.8%) presented with anticipated spontaneous late preterm birth, and 559 (45.2%) were at risk of medically indicated late preterm birth. The distribution of the various indications for late preterm ACS administration in each group is displayed in Table 1. Furthermore, of the 1238 patients included, 656 (53%) delivered <24 hours from administration and thus received only the first dose of betamethasone.

Women at risk of medically indicated late preterm birth had a higher mean maternal age (34 vs 32 years; $P\leq.001$) and BMI (31.4 vs 29 kg/m^2; $P\leq.001$) and were more likely to be of non-Hispanic Black race and Hispanic ethnicity (20% vs 15% and 14.7% vs 10.6%; $P\leq.001$) than in women with anticipated spontaneous late preterm birth (Table 2). In addition, women at risk of medically indicated late preterm birth had higher rates of gestational diabetes mellitus (8.4% vs 3.8%; $P=.001$) and previous pregnancy with medically indicated preterm birth (7.9% vs 2.5%; $P\leq.001$) compared with women with anticipated spontaneous late preterm birth (Table 2). The median gestational age at ACS administration was similar between the 2 groups (Table 2).

Regardless of the indication for late preterm ACS administration, the likelihood of delivery between 2 and 7 days later was 13.3% (165 of 1238). Moreover, delivery between 2 and 7 days after corticosteroid administration was more common in women at risk of medically indicated late preterm birth compared with anticipated spontaneous late preterm birth (23.4% vs 5%; $P\leq.001$) (Table 3). The rate of delivery >7 days after corticosteroid administration and median time interval from corticosteroid administration to delivery were higher in women at risk of medically indicated late preterm birth (28.6% vs 19.7% [$P\leq.001$] and 49.7 vs 10.7 hours [$P\leq.001$]), whereas delivery before 2 days after corticosteroid administration and preterm birth at <37 weeks' gestation were more common in women at risk of spontaneous late preterm birth (75.3% vs 47.9% [$P\leq.001$] and 80% vs 69.8% [$P\leq.001$]) (Table 3).

On multivariable analysis, the likelihood of delivery between 2 and 7 days after corticosteroid administration was significantly higher in women at risk of medically indicated late preterm birth compared with women with anticipated spontaneous late preterm birth (aOR, 5.88; 95% CI, 4.00–9.09) (Table 4). In addition, later gestational age at corticosteroid administration, within the late preterm period, was associated with an increased likelihood of optimal timing (aOR, 1.33; 95% CI, 1.06–1.68) (Table 4).

TABLE 1
Indications for late preterm steroid administration within the study cohort

Indication	ACS administered (n=1238)
Risk of spontaneous late preterm birth	
Suspected preterm labor with intact membranes	316 (25.5)
Ruptured membranes	363 (29.3)
Risk of medically indicated late preterm birth	
Hypertensive disorders of pregnancy	281 (22.7)
Fetal growth restriction	21 (1.7)
Oligohydramnios	71 (5.7)
Intrahepatic cholestasis of pregnancy	23 (1.9)
Nonreassuring fetal status	49 (4.0)
Placenta previa, placenta accreta, or vasa previa	32 (2.6)
Placental abruption	44 (3.6)
Other	38 (3.1)

Data presented as number (percentage).

ACS, antenatal corticosteroid.

Gulersen. Practice patterns of late preterm antenatal corticosteroids. Am J Obstet Gynecol Glob Rep 2021.

Discussion

Principal findings

The results of our study illustrated 2 main findings. First, the likelihood

TABLE 2
Comparison of baseline characteristics between study groups

Characteristic	Risk of spontaneous late preterm birth (n=679)	Risk of medically indicated late preterm birth (n=559)	*P* value
Maternal age (y)	32.0 (29.0–36.0)	34 (31.0–37.0)	<.001
BMI (kg/m^2)	29.0 (25.9–32.7)	31.4 (27.5–35.9)	<.001
Gestational age at ACS administration (wk)	35.7 (35.0–36.3)	35.6 (35.0–36.2)	.89
Race or ethnic group			
Non-Hispanic White	257 (37.8)	205 (36.7)	<.001
Non-Hispanic Black	102 (15.0)	112 (20.0)	
Hispanic	72 (10.6)	82 (14.7)	
Asian	131 (19.3)	76 (13.6)	
Other	80 (11.8)	41 (7.3)	
Unknown	37 (5.4)	43 (7.7)	
Nulliparous	318 (46.8)	287 (51.3)	.32
History of preterm birth			
Spontaneous	77 (11.3)	28 (5.0)	<.001
Medically indicated	17 (2.5)	44 (7.9)	
Gestational diabetes mellitus	26 (3.8)	47 (8.4)	.001

Data are presented as median (interquartile range) or number (percentage), unless otherwise indicated.

ACS, antenatal corticosteroid; *BMI*, body mass index.

Gulersen. Practice patterns of late preterm antenatal corticosteroids. Am J Obstet Gynecol Glob Rep 2021.

of delivery between 2 and 7 days after late preterm ACS administration was low, as only 13.3% (165 of 1238) of our study cohort delivered between that time interval. Second, delivery between 2 and 7 days after ACS administration was more likely in women at risk of medically indicated late preterm birth than in women with anticipated spontaneous late preterm birth, suggesting that delivery between that desired time interval was more common in that group of patients.

Results

This study highlighted the clinical challenge of timing ACSs appropriately in women before anticipated preterm birth. It has been known that the benefit of corticosteroid administration was the greatest between 2 and 7 days after the

TABLE 3
Primary and secondary outcomes

Variable	Risk of spontaneous late preterm birth (n=679)	Risk of medically indicated late preterm birth (n=559)	*P* value
Delivered 2–7 d after ACS	34 (5.0)	131 (23.4)	<.001
Delivered <2 d after ACS	511 (75.3)	268 (47.9)	<.001
Delivered >7 d after ACS	134 (19.7)	160 (28.6)	<.001
Time interval from ACS to delivery (h)	10.7 (5.2–44.6)	49.7 (20.1–96.2)	<.001
Delivered <37 wk	543 (80.0)	390 (69.8)	<.001
Gestational age at delivery (wk)	36.1 (35.3–36.7)	36.4 (35.7–37.0)	.049

Data are presented as number (percentage) or median (interquartile range), unless otherwise indicated.

ACS, antenatal corticosteroids; *IQR*, interquartile range.

Gulersen. Practice patterns of late preterm antenatal corticosteroids. Am J Obstet Gynecol Glob Rep 2021.

TABLE 4
Multivariable logistic regression to evaluate factors associated with optimal timing of ACS administration

Characteristic	Adjusted odds ratio	95% confidence interval	*P* value
Indication for ACS administration—anticipated spontaneous vs medically indicated late preterm birth	0.17	0.11–0.26	<.0001
Gestational age at ACS administration	1.33	1.05–1.68	.02
Maternal age	1.00	0.97–1.04	.9
Body mass index	0.98	0.95–1.01	.2
Race and ethnicity			
Non-Hispanic Black	1.14	0.71–1.84	.6
Hispanic	1.09	0.63–1.90	.7
Asian	1.19	0.72–1.98	.5
Other	1.13	0.59–2.14	.7
Nulliparous	0.69	0.47–1.02	.06
History of spontaneous preterm birth	1.13	0.50–2.55	.8
History of medically indicated preterm birth	1.63	0.80–3.31	.2
Gestational diabetes mellitus	1.04	0.53–2.07	.9

Reference group for race and ethnicity is non-Hispanic White. Maternal age, body mass index, and gestational age at ACS administration were entered into the model as continuous variables.

ACS, antenatal corticosteroids.

Gulersen. Practice patterns of late preterm antenatal corticosteroids. Am J Obstet Gynecol Glob Rep 2021.

initial dose[28] and that corticosteroids should not be administered unless there is substantial clinical concern for imminent preterm birth[16]; however, the timing of corticosteroid administration remained suboptimal.[25–27] This has been demonstrated in women at risk of both spontaneous and medically indicated preterm birth at <34 weeks' gestation. For example, in a cohort of 345 singleton and twin gestations who received betamethasone for treatment of spontaneous preterm birth with intact or ruptured membranes between 24 and 34 weeks' gestation, Adams et al[25] reported that the likelihood of optimally timed corticosteroids (defined in their study as delivery within 7 days of administration) was 20%. In efforts to determine whether timing was more optimal in a separate cohort of 193 singleton and twin gestations at risk of medically indicated preterm birth between 24 and 34 weeks' gestation, Adams et al[25] reported that only 48% of women who received corticosteroids before anticipated indicated preterm delivery gave birth within 7 days of its administration and that optimal timing was more likely when delivery was due to maternal indications (ie, preeclampsia) rather than fetal indication (ie, fetal growth restriction). Our findings of improved corticosteroid timing in women with medically indicated preterm birth compared with those with anticipated spontaneous preterm birth were similar to the studies by Adams et al.[25,26] Lastly, a single-center cohort study of singleton preterm births between 24 and 35 weeks' gestation by Levin et al[27] demonstrated that the likelihood of optimally timed corticosteroids (defined in their sensitivity analysis as delivery between 2 and 7 days after administration) was 27.5%.

Clinical implications

Despite the general similarity of earlier studies in the early preterm period, indicating that corticosteroid timing is often suboptimal, we suggest caution when comparing these studies to ours for several reasons. First, preterm birth becomes more likely as gestational age increases,[33] and thus, only 23.7% (294 of 1238) of our study cohort delivered >7 days after corticosteroid administration, a lower rate compared with the studies reported by Adams et al.[25,26] In addition, this was reflective in our finding that a later gestational age at corticosteroid administration was associated with a higher likelihood of optimal timing. Second, preterm prelabor rupture of membranes was the most common indication for corticosteroid administration in our study, where delivery was usually recommended in the late preterm period rather than expectant management (as in cases before 34 weeks' gestation),[34] increasing the likelihood of delivery within 48 hours after corticosteroid administration, which may be suboptimal. Lastly, our cohort of medically indicated late preterm births included patients with scheduled deliveries before 37 weeks' gestation, a more common event than scheduled delivery <34 weeks' gestation, which may allow for practitioners to time corticosteroid administration more appropriately.

Research implications

The number of patients that completed the course of ACSs before delivery in

our cohort was lower compared with that reported by Gyamfi-Bannerman et al[14] (47% vs 60%) in their randomized trial evaluating the neonatal benefit of corticosteroids in women at risk of late preterm delivery. This may have reflected the eagerness of practitioners to use this intervention in every day practice, which led to suboptimal timing. Furthermore, our cohort included more than 70% of patients who presented with anticipated spontaneous late preterm birth and progressed rapidly to delivery within 48 hours after the first dose of corticosteroid administration, which emphasized the challenge in predicting spontaneous preterm birth that may contribute to suboptimal corticosteroid timing. Nevertheless, future studies investigating the utility of possible predictors of preterm birth, particularly in the late preterm period, and identifying improved clinical criteria that may lead to improved timing of ACSs are needed.

Strengths and limitations

Our study has several strengths. This study investigated the likelihood of delivery in the assumed optimal time interval (between 2 and 7 days) after late preterm ACS administration, which was also stratified by indication to compare women with anticipated spontaneous late preterm birth with those at risk of medically indicated late preterm birth. Our sample size was robust, including more than 1200 singleton pregnancies from 3 different hospitals within a large health system in New York. Moreover, our population was diversified in terms of maternal race, ethnicity, and demographics, making our findings generalizable.

However, this study has several limitations. First, we defined the administration of late preterm ACSs between 2 and 7 days before delivery as an optimal time interval based on data from corticosteroid use in women at risk of preterm delivery at <34 weeks' gestation. Currently, no data exist confirming the optimal time interval for corticosteroid administration for neonates born in the late preterm period, so it remains unclear whether the 2- to 7-day interval indeed carries the greatest benefit to this select population. Nevertheless, this time interval was generally accepted in clinical practice. In addition, the indication for corticosteroid administration was at the provider's discretion in each hospital and extracted from the medical record retrospectively. Although institutional guidelines and consultation with maternal-fetal medicine were present and available to guide practitioners to selecting the appropriate candidates for corticosteroid administration, practice patterns may have varied slightly among the 3 hospitals. Neonatal outcomes were not compared between the 2 groups of late preterm neonates (medically indicated vs spontaneous) as these are impacted by multiple confounding factors. Finally, despite our large sample size, several of the medical indications that applied to corticosteroid administration in our cohort, that is, fetal growth restriction, oligohydramnios, abnormal placentation, and nonreassuring fetal status, were relatively rare, limiting our ability to evaluate the likelihood of optimal timing of each indication within our regression analysis.

Conclusions

We have demonstrated that the likelihood of delivery between 2 and 7 days after ACS administration in women at risk of late preterm birth was low and that delivery between that time interval was more likely in women at risk of medically indicated late preterm birth than in women with anticipated spontaneous late preterm birth. Although any duration of dose exposure has been proven beneficial in reducing short-term neonatal morbidities for this select cohort,[14] the long-term implications of corticosteroid exposure in this period were not fully understood, and recent evidence has suggested possible harm.[35] Thus, selecting the appropriate patient population for whom corticosteroid administration in the late preterm period would be timed appropriately, and result in neonatal benefit is essential to optimize benefits from ACSs while limiting the risks associated with such intervention. ■

REFERENCES

1. Davidoff MJ, Dias T, Damus K, et al. Changes in the gestational age distribution among U.S. singleton births: impact on rates of late preterm birth, 1992 to 2002. Semin Perinatol 2006;30:8–15.
2. Raju TNKR. The "late preterm" birth-ten years later. Pediatrics 2017;139:e2016331.
3. Hamilton BE, Martin JA, Osterman MJ. Births: preliminary data for 2015. Natl Vital Stat Rep 2016;65:1–15.
4. Dudell GG, Jain L. Hypoxic respiratory failure in the late preterm infant. Clin Perinatol 2006;33:803–30.
5. Laptook A, Jackson GL. Cold stress and hypoglycemia in the late preterm ("near-term") infant: impact on nursery of admission. Semin Perinatol 2006;30:24–7.
6. Bhutani VK, Johnson L. Kernicterus in late preterm infants cared for as term healthy infants. Semin Perinatol 2006;30:89–97.
7. McIntire DD, Leveno KJ. Neonatal mortality and morbidity rates in late preterm births compared with births at term. Obstet Gynecol 2008;111:35–41.
8. Kramer MS, Demissie K, Yang H, Platt RW, Sauvé R, Liston R. The contribution of mild and moderate preterm birth to infant mortality. Fetal and Infant Health Study Group of the Canadian Perinatal Surveillance System. JAMA 2000;284:843–9.
9. Petrini JR, Dias T, McCormick MC, Massolo ML, Green NS, Escobar GJ. Increased risk of adverse neurological development for late preterm infants. J Pediatr 2009;154:169–76.
10. Teune MJ, Bakhuizen S, Gyamfi Bannerman C, et al. A systematic review of severe morbidity in infants born late preterm. Am J Obstet Gynecol 2011;205. 374.e1–9.
11. Sharma D, Padmavathi IV, Tabatabaii SA, Farahbakhsh N. Late preterm: a new high risk group in neonatology. J Matern Fetal Neonatal Med 2021;34:2717–30.
12. Porto AM, Coutinho IC, Correia JB, Amorim MM. Effectiveness of antenatal corticosteroids in reducing respiratory disorders in late preterm infants: randomised clinical trial. BMJ 2011;342:d1696.
13. Balci O, Ozdemir S, Mahmoud AS, Acar A, Colakoglu MC. The effect of antenatal steroids on fetal lung maturation between the 34th and 36th week of pregnancy. Gynecol Obstet Invest 2010;70:95–9.
14. Gyamfi-Bannerman C, Thom EA, Blackwell SC, et al. Antenatal betamethasone for women at risk for late preterm delivery. N Engl J Med 2016;374:1311–20.
15. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. Practice Bulletin no. 171: management of preterm labor. Obstet Gynecol 2016;128:e155–64.
16. Committee on Obstetric Practice. Committee Opinion no. 713: antenatal corticosteroid therapy for fetal maturation. Obstet Gynecol 2017;130:e102–9.

17. Liggins GC, Howie RN. A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants. Pediatrics 1972;50:515–25.
18. Roberts D, Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2006;19:CD004454.
19. Amorim MM, Santos LC, Faúndes A. Corticosteroid therapy for prevention of respiratory distress syndrome in severe preeclampsia. Am J Obstet Gynecol 1999;180:1283–8.
20. Block MF, Kling OR, Crosby WM. Antenatal glucocorticoid therapy for the prevention of respiratory distress syndrome in the premature infant. Obstet Gynecol 1977;50:186–90.
21. Carlan SJ, Parsons M, O'Brein WF, Krammer J. Pharmacologic pulmonary maturation in preterm premature rupture of membranes. Am J Obstet Gynecol 1991;164:371.
22. Effect of antenatal dexamethasone administration on the prevention of respiratory distress syndrome. Am J Obstet Gynecol 1981; 141:276–87.
23. Doran TA, Swyer P, MacMurray B, et al. Results of a double-blind controlled study on the use of betamethasone in the prevention of respiratory distress syndrome. Am J Obstet Gynecol 1980;136:313–20.
24. Escobar GJ, Clark RH, Greene JD. Short-term outcomes of infants born at 35 and 36 weeks gestation: we need to ask more questions. Semin Perinatol 2006;30:28–33.
25. Adams TM, Kinzler WL, Chavez MR, Fazzari MJ, Vintzileos AM. Practice patterns in the timing of antenatal corticosteroids for fetal lung maturity. J Matern Fetal Neonatal Med 2015;28:1598–601.
26. Adams TM, Kinzler WL, Chavez MR, Vintzileos AM. The timing of administration of antenatal corticosteroids in women with indicated preterm birth. Am J Obstet Gynecol 2015;212. 645.e1–4.
27. Levin HI, Ananth CV, Benjamin-Boamah C, Siddiq Z, Son M, Friedman AM. Clinical indication and timing of antenatal corticosteroid administration at a single centre. BJOG 2016;123:409–14.
28. Battarbee AN, Ros ST, Esplin MS, et al. Optimal timing of antenatal corticosteroid administration and preterm neonatal and early childhood outcomes. Am J Obstet Gynecol MFM 2020;2:100077.
29. Ring AM, Garland JS, Stafeil BR, Carr MH, Peckman GS, Pircon RA. The effect of a prolonged time interval between antenatal corticosteroid administration and delivery on outcomes in preterm neonates: a cohort study. Am J Obstet Gynecol 2007;196. 457.e1–6.
30. Peaceman AM, Bajaj K, Kumar P, Grobman WA. The interval between a single course of antenatal steroids and delivery and its association with neonatal outcomes. Am J Obstet Gynecol 2005;193: 1165–9.
31. McEvoy C, Schilling D, Spitale P, Peters D, O'Malley J, Durand M. Decreased respiratory compliance in infants less than or equal to 32 weeks' gestation, delivered more than 7 days after antenatal steroid therapy. Pediatrics 2008;121:e1032–8.
32. Waters TP, Mercer B. Impact of timing of antenatal corticosteroid exposure on neonatal outcomes. J Matern Fetal Neonatal Med 2009;22:311–4.
33. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet 2008;371:75–84.
34. Prelabor rupture of membranes: ACOG Practice Bulletin, number 217. Obstet Gynecol 2020;135:e80–97.
35. Räikkönen K, Gissler M, Kajantie E. Associations Between maternal antenatal corticosteroid treatment and mental and behavioral disorders in children. JAMA 2020; 323:1924–33.