Antenatal Late Preterm Steroids (ALPS): Benefits & Barriers

Ronald S. Gibbs, MD
Emeritus Professor, University of Colorado
Professor, Knowles Distinguished Scholar
Stanford University

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Stanford MEDICINE

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Disclosures

- No disclosures regarding commercial interests
- I was the Principal Investigator at the University of Colorado site for the NIH ALPS trial.

Objectives

- Cite the excess morbidity of infants delivering at 34-36 weeks.
- Cite the primary benefit demonstrated in the ALPS study.
- Cite one neonatal complication of ALPS.
- State ACOG/SMFM recommendations for ALPS.
- Implement ALPS recommendations in your practice by identifying and overcoming barriers.

Acknowledgements

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Cynthia Gyamfi-Bannerman, MD, MSc

Columbia University

and

Yasser Y. El-Sayed, MD

Stanford University

Antenatal Late Preterm Steroids

Have you cared for one or more patients who have received ALPS?

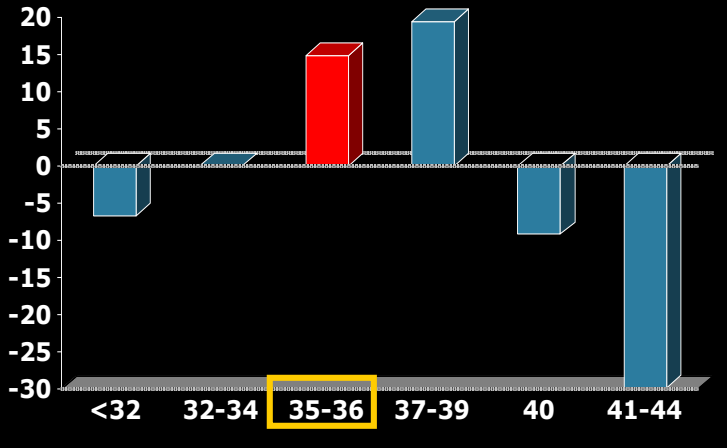
Yes _____ No _____

Antenatal Late Preterm Steroids

Do you feel confident about when to use and when not to use ALPS?

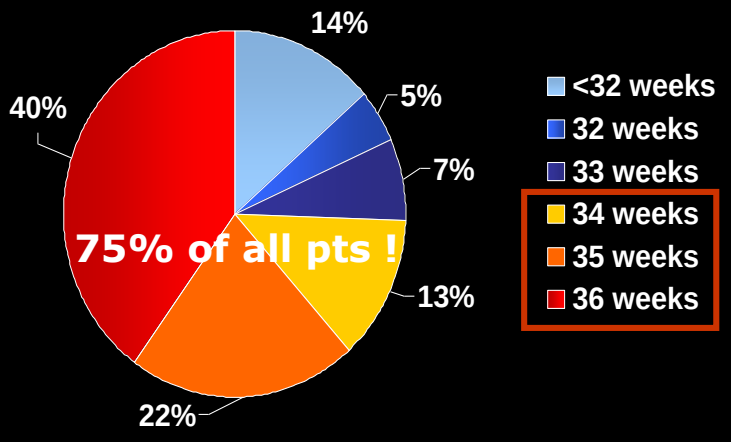
Yes _____ No _____

US preterm births: Change 1992-02



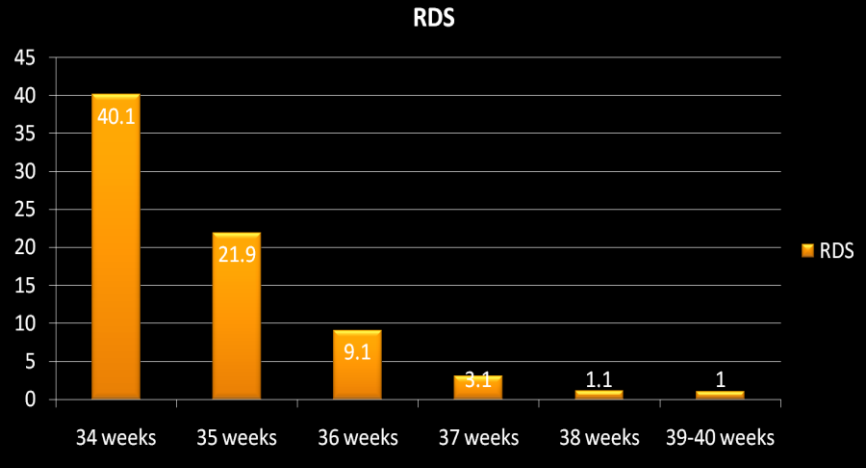
MOD: Davidoff 2005

US Late Preterm Singleton Births



Source: NCHS, final natality data
Prepared by March of Dimes Perinatal Data Center, April 2006.

Adjusted Odds of RDS by GA at Birth



The Consortium on Safe Labor, JAMA 2010;304:419-425.

Morbidity in Late Preterm Infants

- Significant increases compared to 39 weekers in:
  - IVH, grade 1 or 2
  - Culture-proven sepsis
  - Necrotizing Enterocolitis (NEC)
  - Ventilator use

McIntyre & Leveno, *Obstetrics and Gynecology* 2008; 111:35-41

Mortality in Late Preterm Infants

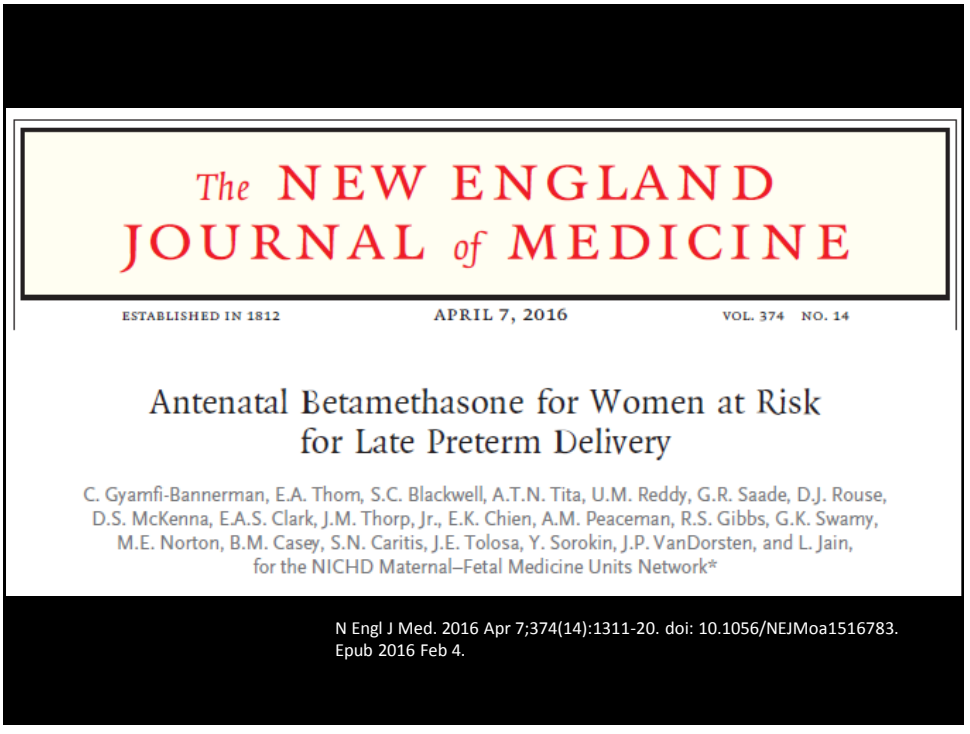
- US singleton births 1995-2002: 30,732,957
- Late Preterm births: 2,221,545 (7.3%)
- Late Preterm deaths: 18,484 (9.8%)
- Mortality in late preterm infants:
  - Early Neonatal (0-6 d) Mortality: 6 x Term
  - Late Neonatal (7-28 d) Mortality: 2 x Term
  - Infant Mortality (birth – 1 year): 3 x Term
- Higher risk persists even after excluding congenital anomalies

Tomashek et al, *J Peds*. 2007;151:460-6

Antecedents to Late Preterm Delivery

Spontaneous (PTL, PPROM)	**Indicated** (NRFHT, severe preeclampsia/HELLP, abruption, previa)	**Elective (NS/NI)** (Repeat C/S, IUGR w/ normal testing, oligo, multiples)
1821/2693	378/2693	494/2693
67.6%	14.0%	18.3%

Gyamfi-Bannerman et al, *AJOG*. 2011;205:456.e1-6



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Antenatal Betamethasone for Women at Risk for Late Preterm Delivery

C. Gyamfi-Bannerman, E.A. Thom, S.C. Blackwell, A.T.N. Tita, U.M. Reddy, G.R. Saade, D.J. Rouse, D.S. McKenna, E.A.S. Clark, J.M. Thorp, Jr., E.K. Chien, A.M. Peaceman, R.S. Gibbs, G.K. Swamy, M.E. Norton, B.M. Casey, S.N. Caritis, J.E. Tolosa, Y. Sorokin, J.P. VanDorsten, and L. Jain, for the NICHD Maternal–Fetal Medicine Units Network*

N Engl J Med. 2016 Apr 7;374(14):1311-20. doi: 10.1056/NEJMoa1516783. Epub 2016 Feb 4.

Objective

To assess whether administration of betamethasone to women likely to deliver in the late preterm period decreased respiratory and other neonatal morbidities

Methods

- Multicenter double-blind randomized, placebo-controlled trial
- 17 MFMU university-based medical centers
  - Both academic and community hospitals
- 2010-2015

Eligibility

- Women with a high likelihood of delivery from 34 0/7 to 36 6/7 weeks
- Specific criteria:
  - Preterm Labor Intact Membranes
    - At least 3 cm dilated or 75% effaced
  - Preterm PROM
  - Indicated preterm delivery
    - Indication at the discretion of the provider
    - Between 24 hours and <7 days after randomization

Exclusion Criteria

- PPROM with active labor
  - >6 CTX/hour or ≥3 cm dilated
- Chorioamnionitis
- Cervical dilation ≥8cm
- Non-reassuring fetal status requiring delivery
- Delivery expected within 12 hours

Exclusion Criteria

- Previous course of antenatal corticosteroids
- Pre-gestational diabetes
  - Unblinding
- Candidate for stress-dose steroids
- Known major fetal anomaly
- Other contraindication to betamethasone

Randomization

- Randomly allocated 1:1 ratio

Betamethasone (12mg) 2mL IM x 2 doses 24 hours apart	Identical placebo 2mL IM x 2 doses 24 hours apart

- Tocolysis was not employed as part of this trial

Primary Outcome

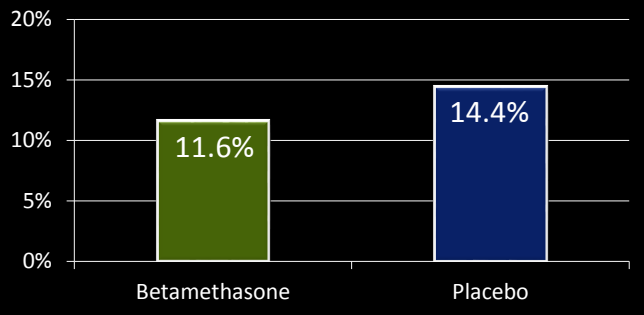
- Composite describing need for respiratory support
  - Oxygen with FiO_2 ≥30% for at least 4 hrs
  - CPAP or high flow nasal cannula for at least 2 hrs
  - Mechanical ventilation
  - ECMO
- All within 72 hrs of birth
- Stillbirth and neonatal death before 72 hrs

Secondary Outcomes

- Severe respiratory morbidity
  - Same composite as primary outcome
    - Oxygen with FiO_2 ≥30% for at least 24 hrs
    - CPAP or high flow nasal cannula for at least 12 hrs

Primary Outcome

- Composite of Need for Respiratory Support



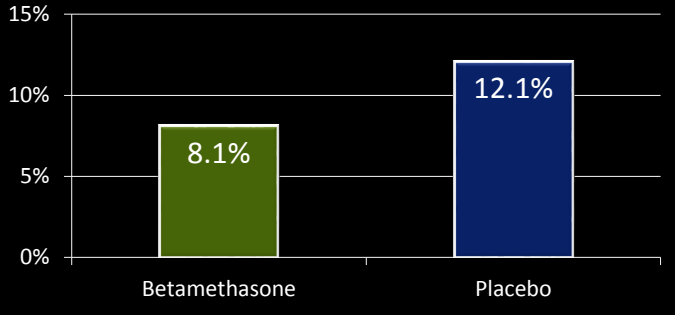
Relative Risk 0.80, 95% CI 0.66-0.97

P=0.02

The number needed to treat = 35

Secondary Outcome

- Severe Respiratory Morbidity



Relative Risk 0.67, 95% CI 0.53-0.84

P<0.001

The number needed to treat = 25

Summary

Antenatal betamethasone given to women at high risk for late preterm delivery significantly decreased the need for respiratory support.

Also decreased relative risk for:

- Prolonged stay in the NICU 11%
- Transient tachypnea of the newborn 33%
- The need for surfactant 41%
- Bronchopulmonary dysplasia 78%
  - Prognostic of childhood chronic lung disease

Summary

- No difference in maternal or neonatal infectious morbidity
- No difference in birth weight or SGA
- Beneficial in the absence of tocolysis
- Hypoglycemia, a known late preterm complication, occurred more frequently after betamethasone exposure
- Associated with shorter Intermediate/NICU stays
- Suggest post-natal glucose assessment
  - Already recommended by the AAP

RESEARCH

OPEN ACCESS

Antenatal corticosteroids for maturity of term or near term fetuses: systematic review and meta-analysis of randomized controlled trials

Gabriele Saccone,[1] Vincenzo Berghella[2]

[1]Department of Neuroscience, Reproductive Sciences and Dentistry, School of Medicine, University of Naples Federico II, Naples, Italy

[2]Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, PA 19107, USA

Correspondence to: V Berghella vincenzo.berghella@jefferson.edu

Additional material is published online only. To view please visit the journal online.

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Accepted: 12 September 2016

ABSTRACT

OBJECTIVE

To evaluate the effectiveness of antenatal corticosteroids given at ≥34 weeks' gestation.

DESIGN

Systematic review with meta-analysis.

DATA SOURCES

Electronic databases were searched from their inception to February 2016.

ELIGIBILITY CRITERIA FOR STUDY SELECTION

Randomized clinical trials comparing antenatal corticosteroids with placebo or no treatment in women with a singleton pregnancy at ≥34 weeks' gestation. Trials on antenatal steroids in women expected to deliver late preterm (34^0-36^6 weeks) and trials given before planned cesarean delivery at term (≥37 weeks) to −1.95), lower maximum inspired oxygen concentration (−0.66%, −0.69% to −0.63%), shorter stay on a neonatal intensive care unit (−7.64 days, −7.65 to −7.64), and higher APGAR scores compared with controls. Infants of mothers who received antenatal betamethasone at 34^0-36^6 weeks' gestation had a significantly lower incidence of transient tachypnea of the newborn (relative risk 0.72, 95% confidence interval 0.56 to 0.92), severe RDS (0.60, 0.33 to 0.94), and use of surfactant (0.61, 0.38 to 0.99). Infants of mothers undergoing planned cesarean delivery at ≥37 weeks' gestation who received prophylactic antenatal corticosteroids 48 hours before delivery had a significantly lower risk of RDS (0.40, 0.27 to 0.59), mild RDS (0.43, 0.26 to 0.72), moderate RDS (0.40, 0.18 to 0.88), transient tachypnea of the newborn (0.38, 0.25 to 0.57), and

BMJ 2016;355:i5044 | doi: 10.1136/bmj.i5044

Obstetric Societies

Society for Maternal-Fetal Medicine

SMFM Statement

smfm.org

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Implementation of the use of antenatal corticosteroids in the late preterm birth period in women at risk for preterm delivery

Society for Maternal-Fetal Medicine (SMFM) Publications Committee

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

COMMITTEE OPINION

Number 677 • October 2016

Committee on Obstetric Practice

This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Committee on Obstetric Practice in collaboration with committee members Yasser Y. El-Sayed, MD, Ann E.B. Borders, MD, MSc, MPH, and the Society for Maternal-Fetal Medicine's liaison member Cynthia Gyamfi-Bannerman, MD, MSc.

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

Antenatal Corticosteroid Therapy for Fetal Maturation

Considerations and Challenges

- ACOG 2016
  - Not indicated in women diagnosed with an intrauterine infection
  - Tocolysis should not be used to delay delivery for antenatal steroids in LP
  - Indicated preterm delivery (i.e severe preeclampsia) should not be delayed

Considerations and Challenges

- ACOG 2016
  - Groups not studied and so unknown benefit
    - Multiple gestation
    - Pregestational diabetes
    - Previous steroid course
  - Overuse of steroids
    - Optimal therapeutic window is 2-7 days
    - Only 20-40% of women delivered in that window following steroids – Adams et al AJOG 2015

SMFM recommendations

1. In women with a singleton pregnancy between 34 weeks 0 days and 36 weeks 6 days of gestation who are at high risk for preterm birth within the next 7 days (but before 37 weeks of gestation), we recommend treatment with betamethasone (2 doses of 12 mg intramuscularly 24 hours apart).
2. In women with preterm labor symptoms in the late preterm period, we recommend waiting for evidence of preterm labor, such as a cervical dilatation of at least 3 cm or effacement of at least 75%, before treatment with betamethasone.
3. In women with late preterm pregnancies receiving betamethasone, we recommend against the use of tocolysis in an attempt to delay delivery to complete the steroid course because it is unclear whether the benefits of betamethasone administration are outweighed by the risks of attempts to delay delivery.

SMFM recommendations

4. In women with late preterm pregnancies with a potential medical indication for delivery, we recommend betamethasone not be given unless there is a definitive plan for late preterm delivery.
5. We recommend that institutions utilize standard guidelines for the assessment and management of neonatal hypoglycemia in late preterm newborns.
6. We recommend against implementation of the Antenatal Late Preterm Steroids protocol for conditions not studied in the randomized controlled trial unless performed as part of research or quality improvement.

Clinical Guide

A reasonable assessment of delivery imminence should guide administration of antenatal steroids in the late preterm period

PTL - 3cm, 75% effaced

and/or

Within 7 days but not for 8-12 hours

Antenatal Late Preterm Steroids

Have you cared for one or more patients who have received ALPS?

Yes _____ No _____

Antenatal Late Preterm Steroids

Do you feel confident about when to use and when not to use ALPS?

Yes _____ No _____

Antenatal Late Preterm Steroids

Does your obstetrical unit have a formal policy about use of ALPS?

Yes _____ No _____ Don't Know _____

Antenatal Late Preterm Steroids

What are/were the barriers to implementing ALPS?

- _____
- _____
- _____
- _____
- _____

Antenatal Late Preterm Steroids

What are/were the barriers to implementing ALPS?

- Remembering who are the candidates for ALPS
- Identifying exactly who is a candidate; judging who is likely to deliver in the “window”
- Worry about side effects
- Too busy with other priorities
- Insurance payment

Antenatal Late Preterm Steroids

How can or did you or your obstetrical service overcome these barriers?

- _____
- _____
- _____
- _____
- _____

Antenatal Late Preterm Steroids

How can or did you or your obstetrical service overcome these barriers?

- Identify a “champion” or team of “champions”
- Use the ACOG/SMFM recommendations as a template
- Prepare formal policy
- ? make ALPS a quality measure