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**Introduction**

Administering betamethasone to individuals who may deliver between 34-36 weeks of gestation decreased the risk of neonatal respiratory complications in the Antenatal Late Preterm Steroid (ALPS) trial. The trial excluded patients with pregestational diabetes and twin pregnancies, and professional societies emphasized caution before recommending late preterm steroids in these populations. Our objective was to understand if the dissemination of the ALPS trial impacted steroid use in these groups.

**Study Design**

We conducted an interrupted time series (ITS) analysis using US natality data between 2014-2018. The primary exposure was the ALPS trial dissemination (February-October 2016), and the outcome was antenatal steroid use. Quarterly steroid administration rates were calculated in the two years before and after the dissemination period.

The ITS model used Poisson regressions to examine the associations of the ALPS trial on steroid exposure in two cohorts: patients delivering at 34-36 weeks gestation with 1) twins, or 2) pregestational diabetes and a singleton. A more detailed description of methods is included in the Online Supplement.

Analyses were performed using Stata 15.1 (StataCorp, College Station, TX). P-values <0.05 were considered statistically significant. The Mass General Brigham IRB determined this was not human subjects research.

**Results**

During the study, 41,181 and 42,162 patients with twin pregnancy and 9,713 and 11,877 patients with pre-gestational diabetes delivered between 34-36 weeks of gestation in the pre- and
post-ALPS trial dissemination periods, respectively. Among twin pregnancies, the observed rate of steroid administration was 19.9% compared to 11.5% (expected based on pre-period trends) in the first quarter after the dissemination period (unadjusted incidence rate ratio (IRR) 1.76, 95% CI 1.58, 1.96; adjusted IRR (aIRR) 1.73, 95% CI 1.58, 1.89) (Figure 1). Similarly, the steroid administration rate was 17.0% (observed) compared to 8.0% (expected) in patients with pregestational diabetes (IRR 2.11, 95% CI 1.64, 2.70; aIRR 2.13, 95% CI 1.57, 2.90). Full model output is included in the Online Supplement.

**Conclusion**

The dissemination of the ALPS trial was associated with increased steroid administration among two populations outside the original inclusion criteria. The Society for Maternal-Fetal Medicine and the American College of Obstetricians and Gynecologists recently emphasized shared decision-making regarding this intervention in twin pregnancies but continued to recommend against its use in people with pregestational diabetes given the unknown benefits and potential risks, such as neonatal hypoglycemia which was noted in the steroid-exposed group in the ALPS trial. Additional studies are indicated to clarify the benefits and risks in these populations and to examine the factors and clinical decision-making contributing to their increased use.

Strengths of our study include its quasi-experimental design and use of US population data. Limitations include its reliance on birth certificate data, which does not record steroid timing or indication. Although some late preterm deliveries may have received steroids <34 weeks of gestation, recommendations regarding steroid use for those <34 weeks did not change. Poor sensitivity for steroid administration in birth certificate data has also been reported.

However, the relative changes in the rates are meaningful assuming that the trial dissemination did not simultaneously impact reporting practices.

Steroid administration rates in the late preterm period increased approximately two-fold among those with pregestational diabetics and twin gestations after the dissemination of the ALPS trial, despite a lack of clear evidence to support its use.

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References


Figure Legend: Expected and observed steroid administration rates among patients with a twin pregnancy (left) and patients with pregestational diabetes (right) by quarter. Models controlled for gestational age, maternal age, race, Hispanic ethnicity, primary payer for delivery admission, and delivering provider type. Circles represent adjusted steroid administration rates in each quarter with their associated 95% confidence intervals. The gray area designates the trial dissemination period, which occurred over 3 quarters from February 2016 (trial’s publication) through October 2016 (practice updates by the American College of Obstetricians and Gynecologists).