**Table S3: Comparing the intention of the research question and methodology (association or causation) with the results, discussion and conclusion (associational or causal language) in observational cohort studies on the antenatal corticosteroids-to-birth interval.**

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| Article | Research question and methodology: association or causation? | Results: association or causation? | Discussion and conclusion: association or causation?  |
| McNamara M, 199827 | association- multiple regression- analysis of variance- multiway contingency table analysis | associationterms used: correlation, relationship, significant difference | causationThey concluded that when controlling for gestational age at delivery, the interval from last steroid dose to delivery did not make a difference in the frequency of RDS. Based on their results, they wrote that they could not support repetitive steroid administration. |
| Vermillion S, 200128 | association- Student-t, chi square, Fisher exact- multiple regression | associationterms used: similar frequencies, not statistically significantly associated | association, with some causationThey concluded that there was no association between delivery between 8 and 14d after a single course of antenatal corticosteroids and increased perinatal morbidity compared with delivery at shorter intervals. “We recognize the limitations of the nonrandomised design of our study; however we tried to limit potential confounding factors (…)”. |
| Smrcek J, 200329 | associationMann-Whitney U, chi square, Fisher exact | associationterms used: significant difference | causationThey write that they studied the effect of time interval between last antenatal corticosteroids and delivery and that the time interval was without influence on RDS.  |
| Sehdev H, 200430 | association- analysis of variance, chi square, Fischer exact- multiple regressionAnd causation: they want to detect an effect. | associationterms used: similar outcomes, nonsignificant differenceAnd causation: “Logistic regression was used to evaluate the effects…” | association |
| Peaceman A, 200531 | association- Student t, Mann Whitney U, chi square, Fisher exact- logistic and Cox regression | associationterms used: rates, not significantly different, not different, associated, association | association (hypothesis generating)“The data suggest that even if premature delivery appears imminent after a prolonged interval from initial antenatal corticosteroids treatment, an empiric rescue course of steroids may not be justified”. |
| Ring A, 200732 | association- Mantel-Haenszel chi-square, Wilcoxon rank sum, Student t- multiple regressionAnd causation: logistic regression is used to adjust for potential confounding | associationterms used: more frequent, ratesAnd causation: “Logistic regression models that were created to control for potential confounders…” | association (hypothesis generating)“Our results and the results of others suggest that a demonstrable diminished effect of antenatal corticosteroids may be dependent on the primary outcome and the specific organ system that is studied”.“Our study demonstrated an association between...”And causation: “There are several limitations of this trial. It was not a randomised trial and, consequently, has the potential biases of observational studies”. |
| Ferguson S, 200933 | association- Student t, chi-square, Fisher exact- multiple regressionAnd causation: logistic regression is used to account for potential confounding | associationterms used: differences, no statistically significant associations in crude rates, reduction in riskAnd causation: ‘associations’ in adjusted rates | association “In our study, no associations ….”“Our study did not demonstrate improvement in rates of…”And a little causation“This retrospective cohort study evaluated the effect of timing of delivery indicated for maternal and/or fetal concerns …” |
| Waters T, 200834 | association- chi-square, Student t- multiple regressionAnd causation: - logistic regression is used to account for potential confounding- sample size calculation for 1/3 risk reduction in RDS incidence: | associationterms used: not statistically different, significantly less frequent, highest rate, no differencesAnd causation: ‘controlling for’, however they report ‘independently associated’ | association“We found that infants with antenatal corticosteroids exposure >7d prior to delivery had a significantly increased rate of RDS compared to newborns who were exposed within the 48h to 7d window, in both univariate and multivariate analysis”.And causation“These findings suggest that the beneficial effects of antenatal corticosteroids are lost after 1 week or more, after controlling for gestational age at delivery. (…) We conclude that the benefits of antenatal corticosteroids are limited in duration for the reduction in RDS”.  |
| Wilms F, 201135 | association- spline functions- multiple regression | causationterms used: effect of the interval, impact of the interval | causation‘We conclude that the effect of antenatal corticosteroids diminishes only in neonates who are born at a gestational age of 28 and 30 weeks, when the time interval between a complete antenatal corticosteroids course and delivery becomes >7d, which results in higher need for intubation and higher chances for the development of chronic lung disease”. |
| Kuk J-Y, 201336 | association- analysis of variance, Kruskal-Wallis, chi-square, Fisher exact- Jonckheere-Terpstra, linear-by-linear association- multiple regressionAnd causation: logistic regression is used to evaluate the effects of potential confounding | associationterms used: not significantly different, less likely, higher, lower, not significantly different, a lower incidence | association (?)“Our data showed that the administration of a single complete course of antenatal corticosteroids was associated with a significantly reduced incidence of RDS in preterm twins born between 24 and 34 weeks of gestation when the time interval between the first steroid dose and delivery was between 2 and 7 days” |
| Melamed N, 201537 | association- analysis of variance, chi-square - multiple regressionAnd causation: logistic regression is used to adjust for potential confounding | associationterms used: statistically significant different, differences, higher rate, to be at higher odds, similar odds, association | association“Some of the beneficial effects appear to be transient because administration of antenatal corticosteroids at greater than 7 days before birth is associated with an increase in the odds of neonatal mortality and morbidity compared with neonates who receive antenatal corticosteroids 1-7d before birth”.“This study provides support for the observation that the effect of antenatal corticosteroids is incomplete at less than 24 hours from administration and may decline after 7 days”. And causation“It is clear that optimization of the timing of antenatal corticosteroids administration may lead to a significant decrease in prematurity-related neonatal mortality and long-term morbidity”.“We cannot rule out the possibility that this association may be secondary to residual confounding or may have occurred by chance”.  |
| Kosinska-Kaczynska K, 201638 | association- Mann-Whitney U, chi-square- logistic regression | associationterms used: differences, significantly moreAnd causation: “In the multiple logistic regression analysis, the only factors significantly influencing the incidence of respiratory complications in twins were delivery following antenatal corticosteroids therapy within 7 days and female sex” | association“We did not observe a significant reduction in RDS rate…”“We found that composite respiratory complications occurred significantly less often…”“There is a relation between neonatal outcome in twins and time interval between antenatal corticosteroids administration and birth. Therefore, a single antenatal corticosteroids course should be administered with caution in order to allow for the completion of treatment without exceeding an interval of 7 days to delivery”.And causation“According to the presented multiple logistic regression analysis, delivery within 7 days from antenatal corticosteroids administration was the independent factor reducing the incidence of respiratory complications in twins”.“The time interval from antenatal corticosteroids to delivery has the greatest impact in the group of singletons born between 28 and 30 weeks (…) No similar study has been conducted in twins yet, but on the basis of our findings we conclude that the effect is similar among twins”. |
| Liebowitz M, 201639 | association- chi-square, Student t- multiple regressionAnd causation: ‘multivariate regression to adjust’, ‘bias corrected confidence intervals’ | associationterms used: relationship, differences, associated, decrease, rateAnd causation: “multivariate regression analyses to adjust for these confounders” | association“We also found that in infants delivering before 28 weeks’ gestation exposure to a two-dose course of antenatal corticosteroids was associated with a decreased incidence of…”“Although we controlled for important confounders (…), there was still the possibility of unmeasured residual confounding” |
| Fuller K, 201740 | association- chi-square, Fisher exact- logistic regression | associationterms used: significant difference, more likely, rate | association“The present study showed that infants delivered 24 to 47 hours after antenatal corticosteroids exposure had lower rates of surfactant, intubation, and intraventricular hemorrhage vs no antenatal corticosteroids, one to 23 hours or 48 or greater of antenatal corticosteroids exposure. All infants exposed to antenatal corticosteroids, regardless of time interval, showed non-significant improvement in overall outcome (…)”.“The present results support the authors’ hypothesis that neonatal outcomes are improved in less than 48 hours after antenatal corticosteroids administration compared to no antenatal corticosteroids (…) With similar, in some instances improved, neonatal outcomes after 24h of antenatal corticosteroids vs 48 or more hours of antenatal corticosteroids the present data supports that indicated deliveries may be performed sooner than 48h after antenatal corticosteroids administration without increasing adverse neonatal outcomes”. |
| Yasuhi I, 201741 | association and causation- univariate regression- multiple regressioncausal research question: “The aim of our study was to evaluate the effects of the antenatal corticosteroids delivery interval on the incidence of RDS (…)” | associationterms used: rate, not significantly different, associated And causation: “In order to control for these confounding variables (…)” | association“In this retrospective study (…) deliveries beyond both seven and 14 days after antenatal corticosteroids administration were found to be significantly associated with an increased incidence of neonatal RDS (with adjusted OR of 12.8 and 64.0, respectively) (…)” |
| Norman M, 201742 | associationtitle: “Association of short antenatal corticosteroid administration-to-birth intervals with survival and morbidity among very preterm infants”- restricted cubic splines- generalized linear modelscausationcausal research question: “What is the shortest administration-to-birth interval of antenatal corticosteroids that promotes survival and decreases neonatal morbidity in very preterm infants?”“Covariables that could be potential confounders of the associations (…)” “We assessed the effect on in-hospital mortality if all infants without antenatal corticosteroids had been administered antenatal corticosteroids less than 3 hours, 3 to 5 hours, and 6 to 12 hours before delivery by rerunning our final 4-category model and subdividing the less-than-24-hours category into these subgroups; we then predicted mortality after setting the population with no antenatal corticosteroids sequentially to the first, second, and third subgroups” *(counterfactual)* | associationterms used: more likely, more often, associated “In a simulation of providing antenatal corticosteroids for the 661 infants in the sample who did not receive antenatal corticosteroids, our model predicted a 26% decrease in mortality of these infants received antenatal corticosteroids at least 3h before delivery (…)” | association and causation“Our findings suggest that infant mortality was rapidly and significantly reduced when antenatal corticosteroids were administered only a few hours before delivery. Infant birth 12 hours following antenatal corticosteroids administration was associated with similar mortality risk as those exposed to antenatal corticosteroids 18 to 48 hours before delivery. Under the assumption of a causal relationship between timing of antenatal corticosteroids and mortality, our simulations showed that if infants with no antenatal corticosteroids prior to delivery received antenatal corticosteroids 6 to 12 hours before delivery, their mortality was estimated to have been reduced by 51%”“An antenatal corticosteroids administration-to-birth interval of 48 hours to 1 week was associated with a significantly reduced risk for severe neonatal brain injury”“(…) residual confounding may have occurred”“In conclusion, our results suggest significant health-promoting effects of antenatal corticosteroids beginning just hours before delivery” |
| Norberg H, 201743 | association- descriptive statistics- Cox proportional hazards regression analysis- multiple Cox proportional hazards regression model and Kaplan-Meier survival analysesAnd causation: “adjusting for factors”causal research question: “The objective of this prospective population-based cohort study was to investigate the impact of the administration-to-birth interval of antenatal corticosteroids on survival of extremely preterm infants”*“Because early surfactant therapy may be in the causal pathway, we ran a sensitivity analysis without surfactant in the model for infant mortality”* | associationterms used: less frequent, lower, proportion, more likely, association, significant difference | association“We found clear associations between timing of antenatal corticosteroids and survival in extremely preterm infants” |
| Lau H, 201744 | association- Student t, Mann-Whitney U- multiple regressionAnd causation: - “adjusting for covariates”- research question: “affects” | associationterms used: significant association, statistically significant difference, more likely | causation“Our results showed that antenatal corticosteroids exposure in preterm neonates significantly reduce the incidence of RDS and oxygen therapy requirement. There was a benefit of administrating corticosteroids within 7 days of delivery (…)”“Our study is a retrospective review which limits the analysis on cause and effect relationship between the factors and outcomes” |
| Frändberg J, 201845 | association- chi-square, Mann-Whitney U, analysis of variance, Kruskal-Wallis- multiple regressionAnd causation: “adjusted for confounders” | associationterms used: differences, significantly different, more likely | association and causation“An antenatal corticosteroids delivery interval more than seven days was associated with an increased risk of neonatal respiratory morbidity and a prolonged stay in the neonatal intensive care unit”“The timing of antenatal corticosteroids influences the likelihood of benefit from treatment”“The present study and recent findings by Norberg et al suggest a change in clinical practice towards offering antenatal corticosteroids to those most likely to deliver within seven days”reviewer bias, selection bias |

**Abbreviation:** RDS = respiratory distress syndrome. Green = associational language. Red = causal language.