Outline of a multi-county randomized trial of antenatal corticosteroids for women at risk of imminent preterm birth in health facilities in low-resource settings to improve newborn outcomes

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ACS: current evidence

• Updated Cochrane review (>20 RCTs, most in high income settings)
  32% fewer neonatal deaths (RR 0.68, CI 0.58–0.80)
  35-55% reduction in morbidity (RDS, IVH, NEC)

• A community-based, cluster-RCT in Guatemala, Kenya, Argentina, Zambia, India, Pakistan
  12% more neonatal deaths (RR 1.12, CI 1.02–1.22) overall
  (No difference in <5th centile (RR 0.96, CI 0.87–1.06)

• LMIC settings: Equipoise
Research Question

Are antenatal corticosteroids safe and efficacious, when given to women with (a) live fetus(es) at risk of imminent preterm birth between 26+0 and 33+6 weeks gestation for preventing neonatal mortality in hospitals in resource-limited LMIC settings?
Primary objectives:

• To compare the effect of dexamethasone with that of identical placebo on baby’s survival when given to women at risk of imminent preterm birth between 26⁻⁰ and 33⁺⁶ weeks gestation in LMIC facilities.

• To compare the effect of the above intervention on maternal infections.
Secondary objectives:

• To compare the effect of the intervention on:
  – neonatal morbidity outcomes
  – maternal mortality and morbidity
Population:

- Pregnant women from 26+0 to 33+6 weeks gestation with live fetus(es) in whom birth is planned or expected within 48 hours.
Intervention and Comparison:

INTERVENTION

- Most enrolled women expected to have a single course of IM dexamethasone:
  - 6mg IM dexamethasone every 12 hours, to a total of 4 doses (or until delivery occurs, whichever comes first).

- A second course of IM dexamethasone to be administered (ensuring initial allocation treatment) if an enrolled woman does not deliver within 7 days after the initial dose, is still at high risk of preterm birth in the next 48 hours.

COMPARISON

Identical placebo, using identical regimen as for intervention.
Primary Outcomes:

• **Neonatal death:** Death of a *liveborn* neonate within 28 completed days of life

• **Death after enrolment:** Death of the fetus after enrolment or death of a liveborn neonate within 28 completed days of life

• **Maternal infection:** fever, chorioamnionitis, postpartum endometritis, wound infection, non-obstetric infection
Secondary outcomes

• Neonatal morbidity
  – Severe RDS
  – major resuscitation at birth
  – interventricular hemorrhage
  – hypoxic ischemic encephalopathy
  – Hypoglycemia
  – severe hypothermia
  – severe neonatal infection

• Maternal morbidity and mortality

• Care received by the neonate
Study sites and investigators

- Bangladesh (Sylhet): A Baqui, SB Chowdhury, M Shahidullah
- India (Belgaum): S Goudar
- Pakistan (Rahim Yar Khan): S Ariff
- Kenya (Nairobi): J Kinuthia, Z Qureshi, F Were
- Nigeria (Ile-Ife): EA Adejuyigbe, O Kuti
- Nigeria (Ibadan): Al Ayede, B Fawole