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): AI Ayede, B Fawole