Objective
The HIV pandemic affects 36.9 million people worldwide, of whom 1.5 million are pregnant women. 91% of HIV-positive pregnant women reside in sub-Saharan Africa, a region that also has very poor perinatal outcomes. We aimed to establish whether untreated maternal HIV infection is associated with specific perinatal outcomes.

Methods
We performed a systematic review and meta-analysis of the scientific literature by searching nine electronic literature and clinical trial databases, using search terms for HIV and perinatal outcomes, for studies published from Jan 1, 1980, to Dec 7, 2014. Two authors independently reviewed the abstracts retrieved, identified relevant studies, and extracted the data. We investigated the associations between maternal HIV infection in women naive to antiretroviral therapy and 11 perinatal outcomes: preterm birth, very preterm birth, low birthweight, very low birthweight, term low birthweight, preterm low birthweight, small for gestational age, very small for gestational age, miscarriage, stillbirth, and neonatal death. We included prospective and retrospective cohort studies and case-control studies reporting perinatal outcomes in HIV-positive women naive to antiretroviral therapy and HIV-negative controls. We used a random-effects model for the meta-analyses of specific perinatal outcomes. We performed subgroup and sensitivity analyses and assessed the effect of adjustment for confounders. This systematic review and meta-analysis is registered with PROSPERO, number CRD42013005638.

Results
Of 60750 studies identified, we obtained data from 35 studies (20 prospective cohort studies, 12 retrospective cohort studies, and three case-control studies) including 53623 women. Our meta-analyses of prospective cohort studies show that maternal HIV infection is associated with an increased risk of preterm birth (relative risk 1.50, 95% CI 1.24-1.82), low birthweight (1.62, 1.41-1.86), small for gestational age (1.31, 1.14-1.51), and stillbirth (1.67, 1.05-2.66). Retrospective cohort studies also suggest an increased risk of term low birthweight (2.62, 1.55-4.31) and preterm low birthweight (3.25, 2.12-4.99). The strongest and most consistent evidence for these associations is found in sub-Saharan Africa. No association was identified between maternal HIV infection and very preterm birth, very small for gestational age, very low birthweight, miscarriage, or neonatal death, although few data were available for these outcomes. Correction for confounders did not affect the significance of these findings.

Conclusion
Maternal HIV infection in women who did not receive antiretroviral therapy is associated with preterm birth, low birthweight, small for gestational age, and stillbirth, especially in sub-Saharan Africa. Research is needed to assess how antiretroviral therapy regimens affect these perinatal outcomes.