Table S1. Comparison of study designs across maternal influenza immunization trials in Mali, Nepal, and South Africa.

	Trial site—study design and methods		
	Mali	**Nepal**	**South Africa**
Design	Randomized, controlled, observer-blind trial	Randomized, placebo controlled, community-based trial	Randomized, double-blind, placebo-controlled trial
Study population	Pregnant women receiving prenatal care at six referral centers and community health centers in Bamako. The community health centers are staffed by trained midwives while the referral centers have an obstetrician on staff	Women who are or who become pregnant in 9 Village Development Committees in Sarlahi District, Nepal. The healthcare centers within the Village Development Committees are staffed by traditional birth attendants	HIV-uninfected women accessing prenatal care at Chris Hani-Baragwanath Hospital or at one of four community-based antenatal clinics in Soweto region. The community-based clinics are staffed by midwives; in addition, women identified as having complicated or high-risk pregnancies would be assessed by medical doctors, including obstetricians at the hospital
Stated primary objectives	To compare the incidence of laboratory-confirmed influenza (LCI) among infants up to 6 months of age born to mothers immunized with trivalent influenza vaccine (TIV) during the 3rd trimester of pregnancy versus infants born to mothers who received meningococcal conjugate vaccine (MCV) during the 3rd trimester of pregnancy (intention-to-treat (ITT) comparison) To compare the incidence of LCI among infants up to 6 months of age born to mothers immunized with TIV during the 3rd trimester	To compare the incidence of laboratory confirmed influenza illness episodes among newborn infants (through 6 months of age) born to women randomized to receive either influenza vaccine or control during pregnancy To compare the incidence of low birthweight (<2500 g) of newborn infants born to women randomized to receive either influenza vaccine or control during pregnancy	To determine the efficacy of TIV vaccination of pregnant women against laboratory-confirmed influenza illness, due to wild-type influenza strains which are homologous to vaccine-strains, in their infants up to 24 weeks of chronological age To evaluate the immunogenicity of TIV in pregnant women vaccinated between 20–36 weeks of gestational age

	Trial site—study design and methods		
	Mali	**Nepal**	**South Africa**
	of pregnancy versus infants born to mothers who received MCV during the 3rd trimester of pregnancy, for infants born to women immunized ≥14 days prior to delivery	To compare the incidence of influenza-like illness (ILI) episodes among pregnant women (through 6 months postpartum) in women randomized to receive either influenza vaccine or control during pregnancy	
Enrollment	Third trimester of pregnancy (28 weeks or later)	17–34 weeks of gestation	≥20 to <36 weeks of gestation
Follow-up	Enrollment to infant 6 months of age	Enrollment to infant 6 months of age	Enrollment to infant 24 weeks of age
Major maternal eligibility criteria	In third trimester of pregnancy, intends to reside within study area until her newborn infant is 6 months of age	Lives within one of 9 selected VDCs; between 17 and 34 weeks gestation	≥18 to <39 years of age; gestational age 20–<36 weeks, HIV-1 uninfected
Major maternal exclusion criteria	History of severe influenza vaccine reaction, Guillain-Barre syndrome, egg allergy, chronic medical condition; known active infection with HIV, hepatitis B, or hepatitis C; complications with ongoing pregnancy (preterm labor, placental abruption, rupture of membranes, known major congenital anomaly, preeclampsia); acute illness or high temperature within 72 h of vaccination [temporary exclusion criterion]; receipt of any other vaccine excluding tetanus toxoid	Does not intend to deliver child within 9 VDCs in study area; already received current influenza vaccine; allergic to any component of vaccine; >34 weeks gestation. Also, excluded from primary analyses if delivers <2 weeks following receipt of study vaccine	Receipt of TIV (other than through the study) during current influenza season documented by medical history/record; receipt of any live licensed vaccine in last 28 days or inactivated licensed vaccine (except for TT) in last 14 days prior to study vaccine; receipt of non-licensed agent (e.g., vaccine, drug) in last 28 days before vaccination or plans to receive such before delivery; any significant acute illness and/or oral temperature (≥38 °C) in last 24 h prior to study entry

	Trial site—study design and methods		
	Mali	**Nepal**	**South Africa**
	within 2 weeks (inactivated vaccines) or 4 weeks (live vaccines and meningococcal A conjugate vaccine); intends to travel out of study area in the 40 days after delivery; receipt of immunoglobulins or any blood products within 30 days of study vaccine; chronic usage of immunosuppressants or other immune-modifying agents within 90 days of study vaccine		[temporary exclusion criterion]; use of anti-cancer systemic chemotherapy or radiation in last 48 weeks before study enrollment or has immunosuppression as a result of underlying illness or treatment; long-term use of glucorticoids or high-dose inhaled steroids within 12 weeks of study entry; receipt of corticosteroids for preterm labor within 14 days before study entry; receipt of immunoglobulin or other blood products within 12 weeks before enrollment or is scheduled to receive such during pregnancy or for first 24 weeks after delivery; receipt of IL-2, IFN, GMCSF or other immune mediators within 12 weeks before enrollment; uncontrolled major psychiatric disorder; history of severe adverse reaction to previous TIV; pregnancy complications in current pregnancy (e.g., preterm labor, hypertension)
Randomization	1:1 randomization at each health center, using blocks of size divisible by 2	1:1 randomization, blocked by VDC (Cohort 1) or by VDC and gestational age at vaccination [17–24 weeks, 25–34 weeks] because timing of vaccination not	1:1 randomization, in blocks of 30 by enrollment site

	Trial site—study design and methods		
	Mali	**Nepal**	**South Africa**
		randomly/uniformly distributed (Cohort 2)	
Blinding	Observer-blinded (subjects and those involved in clinical surveillance for influenza and adverse reactions blinded), vaccination nurses not blinded	Only vaccinator will be un-blinded (will not be involved in assessment of reactogenicity or illness)	The statistician was responsible for generation of the randomization codes and therefore, was not blinded; however, the statistician was not involved in subject enrollment, case ascertainment or any other component of the study. All remaining staff in the data management team was blinded