Text S2: Low Accrual

The original estimate of the sample size was based on a pilot study we conducted in Nigeria in 2004-2006, with an adverse outcome rate of 9% [1] We used a 5% incidence of severe OH taken from the literature.[2-4] We applied what we thought was a conservative 4.5% incidence rate of OH to assessments of delivery rates and transfer rates occurring in Harare and Lusaka facilities in 2005. A sample size of 2400 women was calculated based on a reduction in incidence from 9.0% to 4.5% in extreme adverse outcome at 20 clinics, of varying sizes, 80% power, two-sided type 1 error rate of 5% and an intra-cluster correlation coefficient of 0.01.[5] Achieving this target required enrolling approximately 3.3 women per clinic per month over 3 years, which we felt was possible based on the assessment of delivery rates in Harare and Lusaka.

By the time data collection for the RCT began in 2009, two major events happened which affected both the overall pool of delivering women and actual incidence of PPH. The size of the population in Harare was reduced by the mass forced migration of shack dwellers in the peri-urban sites served by our primary health care clinics, Operation Murambatsvina, which affected more than 700,000 people.[6] The incidence rate of PPH in all sites decreased, perhaps due to the uptake of pre-delivery uterotonic prophylaxis by the midwives at the PHC level, which was not routinely performed during the assessment phase (2005). Prophylactic uterotonics have been demonstrated to decrease PPH by up to 60%.[7-9] By 2009, over 96% of all women delivering at PHCs received prophylaxis. Finally, as has been noted in other studies, participation in research trials, which emphasize standardized care and enhance data collection and recording of events has been shown to improve outcomes, even in the control arms.[10] In our study, there was an emphasis on prevention of PPH and training on the standardized protocol for management of PPH and prevention/management of shock; the clinical study staff participated in at least 3 training sessions (before each of the study phases), as well as frequent refresher trainings by research staff throughout the trial (Text S3, Table S1).

By 2008, when we were consistently below the expected rate of enrollment, we attempted to increase enrollment by adding the sites in the Copperbelt, 14 PHCs and two RHs, by increasing study monitoring of enrollment criteria, enrollment procedures and data forms, by continual retraining of low enrolling individual clinician/data collectors and PHCs, and by monitoring admissions to the RH for eligible patients sent from intervention or control clinics. However, these efforts never brought the per clinic mean enrollment to greater than 0.8 cases per clinic per month.

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