**Supplement to: Effectiveness of intermittent screening and treatment of malaria in pregnancy on maternal and birth outcomes in selected districts in Rwanda: A cluster randomized controlled trial**

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**Supplemental methods**

The cluster randomized design was selected for logistic reasons, to enable the study to be carried out programmatically. All public health centers in the districts (8 in Huye, 6 in Kamonyi) were included to ensure representation of different health facilities, malaria caseloads, and geographic location. Within each district, facilities were pair-matched based on ANC client load and geography (ie., rural/ urban); one facility in each of the seven pairs was randomly allocated (by coin toss) to ISTp and the other to the control arm. With the exception of the laboratorians, who were blinded to arm, concealment was not possible given the nature of the intervention, however, all of the main outcomes were based on objective measures (birthweight, hemoglobin, malaria infection).

In control health centers, only women reporting fever were tested for malaria; all were tested by microscopy. Treatment with quinine or artemether-lumefantrine was provided according to national guidelines if microscopy positive. In the intervention sites, all women were tested for malaria with the SD BIOLINE™ Malaria Ag P.f./PAN (05FK67) RDT (Standard Diagnostics, Inc., Yongin-si, Gyeonggi-do, Korea; panel detection score, a combined measure of positivity rate incorporating inter-test and inter-lot consistency, of 94.0 at 200 parasites/ml)[1] at each regularly scheduled visit, regardless of symptoms, and treated per national guidelines if the RDT was positive. This RDT is reported by the manufacturer to have a sensitivity of 99.7% and specificity of 99.5% for detections of *P. falciparum* HRP2 (<https://itama.co.id/wp-content/uploads/2021/11/SD-Bioline-Malaria-Ag-RDT-Series.pdf>). In field testing, sensitivities from 25-96.2%[2] have been reported, with specificity 77-90%, positive predictive value 67-70%, and negative predictive value 35-78%.[3] Women presenting symptomatically at an unscheduled visit in either arm underwent microscopy and were treated accordingly.

At the time of delivery, maternal peripheral and placental blood samples were collected on filter paper for malaria testing in all facilities. Neonatal parameters (birth outcome [alive/ stillborn/ neonatal death], birthweight [measured to the nearest 100 gm], and prematurity [by last menstrual period and fundal height measurement]) were recorded.

**Supplemental results**

Overall, at delivery, 15.2% of women had evidence of placental malaria by PCR, 10.4% by peripheral blood PCR, and 4.4% by peripheral blood RDT. The RDT thus had a sensitivity of 21.6%, specificity of 98.2%, positive predictive value (PPV) of 68.3%, and negative predictive value (NPV) of 87.5% compared to placental PCR, and sensitivity of 30.4%, specificity of 98.1%, PPV of 65.1% and NPV of 92.5% compared to peripheral blood PCR (Supplemental Table).

*Supplemental Table. Results of RDT compared to PCR*

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Malaria detected by placental PCR** | | |
| **RDT at delivery** | **Positive** | **Negative** | **Total** |
| **Positive** | 41 (21.6%) | 19 (1.79%) | 60 |
| **Negative** | 149 (78.4%) | 1040 (98.2%) | 1189 |
| **Total** | 190 | 1059 | 1249 |
|  | **Malaria detected by PCR from maternal capillary blood at delivery** | | |
| **RDT at delivery** | **Positive** | **Negative** | **Total** |
| **Positive** | 41 (30.4%) | 22 (1.85%) | 63 |
| **Negative** | 94 (69.6%) | 1164 (98.2%) | 1258 |
| **Total** | 135 | 1186 | 1321 |

**Supplemental References**

1. World Health Organization. Malaria rapid diagnostic test performance: summary results of WHO product testing of malaria RDTs: round 1-8 (2008–2018). . Geneva: World Health Organization, **2018**:Licence: CC BY-NC-SA 3.0 IGO.

2. Gendrot M, Madamet M, Fonta I, et al. Comparative Assessment of the Sensitivity of Ten Commercial Rapid Diagnostic Test Kits for the Detection of Plasmodium. Diagnostics (Basel) **2022**; 12.

3. Ali IM, Nji AM, Bonkum JC, et al. Diagnostic Accuracy of CareStart™ Malaria HRP2 and SD Bioline Pf/PAN for Malaria in Febrile Outpatients in Varying Malaria Transmission Settings in Cameroon. Diagnostics **2021**; 11:1556.