Supplemental file S4: Main reasons of study drop out in RECIPAL cohort

Recruitment of WRAs was stopped in September 2016, when only 1,214 WRAs had been included. The recruitment period lasted 9 months more than was planned in the protocol (27 months vs. 18 months), but it could not be extended further because of financial reasons. Besides, because of constraints related to both the study design and the local socio-cultural context, a noticeable proportion, 36.5 % (444/1214) of WRAs did not complete the pre-conceptional follow-up. At the end, both the number of WRAs and the number of pregnant women included in the RECIPAL study were far lower than was planned. Difficulties in recruiting women, and the reasons of drop out before and during pregnancy were the following:

✋ Constraints related to the study design

To be included in RECIPAL, women should not have planned to travel for more than 2 months within the next 18 months. However, many women travelled during their follow-up. Women with three successive missing visits or with two successive missing visits with a positive pregnancy test at their return were excluded from the study (see Supplemental file S3). As described in the flow chart diagram, among women with incomplete pre-conceptional follow-up, 31.1% (138/444) moved outside the study area for more than two months and had to be excluded. Sô-Ava district is a lakeside city with fishing as principal activity. During the period of high fishing activity (~ 3 to 4 months/year), many women travel by ship to Makoko city in Nigeria for fish trade. In RECIPAL, 63.2% (86/138) of women who travelled went to Nigeria as final destination.

One of the main constraints related to the study design was the long duration of the pre-conceptional follow-up. Among the WRAs who withdrew their informed consent, 36% (98/272) of them reported study fatigue and disappointment of not being pregnant. No drugs or interventions were administered/implemented by the project to help women to conceive, only medical advices and clinical examination in case of symptoms suggestive of genital infection were provided.

During pregnancy, the main constraint was related to the number of ANC visits. Indeed, nine ANC visits were scheduled. At each visit, a thick blood smear was performed using capillary blood, except at the 2nd and 6th ANC visit when venous blood was collected. The mean number of ANC visits (including both scheduled and unscheduled visits) was 8.1 (SD ±2.8;

range: 1-15). Although most women were globally satisfied with the RECIPAL follow-up, some of them withdrew their informed consent because of too frequent ANC visits.

✋ African socio-cultural realities

Sixty-four percent of women (174/272) refused to continue participating in the study because of rumours about blood and placental samples collection, as well as suspicion regarding medical care provided free of charge for the woman. Indeed, at the beginning of the study false rumours circulated about the quantity and number of times blood was collected, and its use for religious purposes. Despite regular sensitization campaigns in the villages, project endorsement by the local (health) authorities and religious leaders, as well as organization of visits to our laboratory, rumours could not be completely eradicated. The fact that a high proportion of women were illiterate (> 70%) and from Toffin ethnicity (fears of foreign populations) contributed to the spread of rumours.

Despite the usefulness of the placenta for biomedical research, personal, socio-economic and cultural factors undermine the willingness of mothers to freely donate their placentas for research purpose, especially in SAA [1]. In Africa, including Benin, there are strong emotional, religious and cultural ties to how placentas are disposed. Indeed, a careless handling of the placenta is associated with a risk of infertility, illness and death in the newborn baby [2,3]. In RECIPAL, after a small piece of placenta was drawn for malaria histology and 4mL placental blood was collected for malaria screening, the placenta was immediately returned to the woman. Information—on why and how placenta will be collected—was provided to the woman and her family throughout the follow-up. Despite these precautions, placenta collection remained one of the main reasons for consent withdrawal.

The social pressure exerted by the family members was another issue in RECIPAL study. As far as possible, women's partners and family members (particularly, the women's mother-in-law) were involved at the various stages of follow-up. For many women, family agreement was required for their participation in the study and for monthly follow-up at the maternity clinic until delivery. Besides, in the RECIPAL study, women benefited from free management of any diseases related to the pregnancy—detected either as part of scheduled follow-up or during emergency visits—, free ANC visits and delivery. Eighteen percent (8/45) of consent withdrawals were due to the fact that the family-in-law judged the woman's partner unable to take care of their daughter correctly because of free antenatal care.

✋ Pregnancy cohort attrition

In the final cohort, 32.1% (132/411) of pregnant women did not complete the follow-up, mainly because of spontaneous abortion (51.5%, 68/132) and informed consent withdrawal (34.1%, 45/132). Reasons for consent withdrawal have been given above. There are few data available on spontaneous abortions, particularly in SSA countries, where they are neither detected nor reported. In RECIPAL, the prevalence of spontaneous abortions was unexpectedly high (16.5%, 68/411), with more than half (50.7%, 34/68) of cases occurring before 6 weeks of gestation.

References:

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3 Herlihy JM, Shaikh A, Mazimba A, *et al.* Local Perceptions, Cultural Beliefs and Practices That Shape Umbilical Cord Care: A Qualitative Study in Southern Province, Zambia. *PLoS ONE* 2013;**8**.