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Malaria in Pregnancy: Intermittent Preventive Treatment

A cost-effective intervention for preventing maternal and newborn mortality

February 2013

Plasmodium falciparum malaria during pregnancy can result in negative outcomes in maternal and child health. In malaria stable transmission areas in Africa, approximately **25 million pregnancies are exposed every year to the infection**. An estimated 10,000 of these women and 200,000 of their infants die as a result of malaria infection during pregnancy, and severe malarial anaemia contributes to more than half of these deaths.

Malaria infection during pregnancy is one of the contributors to neonatal mortality, mostly through low birth weight (LBW) and prematurity and by causing maternal anaemia or maternal malaria infection (placental parasitaemia). In areas of moderate-to-high malaria transmission, the current World Health Organization (WHO) recommended strategies[1] include both preventive and curative measures: the **intermittent preventive treatment during pregnancy with sulfadoxine pyrimethamine (IPTp-SP)** to prevent asymptomatic infections, insecticide treated bed nets (ITNs) and effective case management for malaria illness and anaemia among pregnant women. In several countries in Africa, some *P. falciparum* parasites carry mutations linked to SP resistance which are associated with therapeutic failure to SP. But IPTp with SP remains effective in areas where a high proportion of *P. falciparum* parasites carry these mutations and hence should still be administered to women in such areas.

IPTp-SP administered through routine antenatal care (ANC) has been proven to be very efficacious in reducing clinical malaria during pregnancy and neonatal mortality. Since 2010 there is confirmatory evidence[2] from malaria prevention trials in pregnancy of a significant effect of the intervention on infant survival during the first year of life. IPTp-SP, given 2 or 3 times during pregnancy to women residing in areas of stable malaria transmission reduces the risk of LBW in babies and hence increases the probability of child survival. The effect of malaria prevention with IPTp on survival during the first year of life is of critical importance: **IPTp can reduce neonatal mortality by more than 60%.** IPTp-SP is currently health policy in several African countries, and is being deployed and scaled up through reproductive health programmes. However, in many African countries the uptake of this preventive tool is still far from full coverage of pregnant women at risk of malaria: it is estimated[3] that only 25% of pregnant women received at least 1 dose of IPTp.

When is the IPTp-SP intervention cost-effective?

Although IPTp-SP has been recommended since 1998, until recently, there was little and incomplete information[4] on the economic evaluation of this strategy. There is a need to conduct economic evaluations of malaria prevention in specific groups (i.e. pregnant women and infants) to inform health decision-makers on how to determine the allocation of very limited healthcare resources. **A cost-effectiveness study**[5] comparing the administration of IPTp-SP plus the use of ITNs with using only ITNs, was conducted among 1,000 pregnant women enrolled at the antenatal care services in a

[1] http://www.who.int/malaria/iptp_sp_updated_policy_recommendation_en_102012.pdf

[2] Menéndez C, Bardají A, Sigauque B, Sanz S, Aponte JJ, et al. (2010) Malaria Prevention with IPTp during Pregnancy Reduces Neonatal Mortality. PLoS ONE 5(2): e9438. doi:10.1371/journal.pone.0009438

[3] Van Eijk A, Lancet Inf Dis 2011 Coverage of malaria protection in pregnant women in sub-Saharan Africa: a synthesis and analysis of national survey data. The Lanct. Vol.11.March

[4] All previously published economic evaluations of IPTp-SP used surrogate indicators of infant mortality and of maternal mortality and morbidity to calculate disability adjusted life years (DALYs).

[5] Sicuri E, Bardají A, Nhampossa T, Maixenchs M, Nhacolo A, et al. (2010) Cost-Effectiveness of Intermittent Preventive Treatment of Malaria in Pregnancy in Southern Mozambique. PLoS ONE 5(10): e13407. doi:10.1371/journal.pone.0013407.

Key Findings:

-The intermittent preventive treatment of malaria in pregnancy with sulphadoxine-pyrimethamine (IPTp-SP) has proved to be a **highly cost-effective strategy** for both prevention of maternal malaria and reduction of neonatal mortality when administered in the context of routine ANC[9] in Mozambique.

- IPTp-SP remains cost-effective for preventing **clinical malaria in pregnant women** even with significant increases[10] in drug and other intervention costs (i.e. health staff) when compliance with ITNs is high, ANC attendance is above 37% and the protective efficacy of the SP is above 15%.

-IPTp-SP remains highly[11] cost-effective to prevent **neonatal mortality** in the following scenarios: significant increases in drug cost (up to 11U$ per dose) and other intervention costs (personnel costs per dose delivered below 7.90 US$), decrease in the number of deaths averted (up to 4.66%), ANC attendance higher than 37.5%.

-The **protective efficacy** of IPTp-SP is the factor that most contributes to the cost-effectiveness of the IPTp-SP intervention on both clinical malaria and on neonatal mortality. Thus, improvements in the protective efficacy of the drug used for IPTp would have a strong positive impact in the cost-effectiveness of the intervention.

-Protective efficacy of IPTp-SP also showed strong association with **health system's savings** and **households' savings.**

rural area of Southern Mozambique in the context of a clinical trial[6]. Mozambique is one of the countries in the African region with the highest malaria burden.[7] The study compared **costs** (i.e. IPTp intervention costs such as drug costs or health staff, household and health system costs of malaria treatment during pregnancy) and **health effects** resulting from IPTp administration on maternal clinical malaria and neonatal survival (i.e. number of out/inpatient episodes averted, number of maternal and neonatal deaths averted, number of Disability Adjusted Life Years - DALYs[8]- averted) and assessed the extent to which the IPTp-SP intervention can provide value for money. In addition, **cut-off values** of costs, health effects, burden of malaria during pregnancy and ANC attendance, beyond which the intervention is no longer cost-effective as well the **main factors** affecting the **economic outcomes** were estimated.

Conclusions

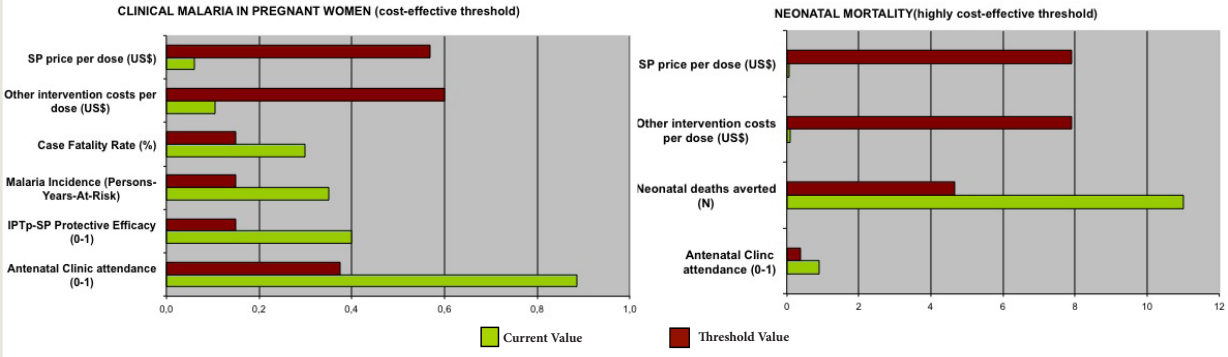
• IPTp-SP is a cost-effective public health measure to prevent malaria in pregnancy that should remain a priority prevention strategy across stable malaria transmission countries.

• Malaria prevention in pregnancy is a good investment when provided through the antenatal care services that yields benefits that accrue for mothers, their newborns, communities and society at large. And the investment is modest in relation to the dramatic return it guarantees preventing premature death and future disability.

• The study assessed that safe and more efficacious drugs than SP, despite being remarkably more expensive, would improve the cost-effectiveness of the intervention.

• These findings are likely to hold for other similar settings in the African region where IPTp-SP is implemented through ANC visits.

Cut-off values for determination of IPTp-SP cost-effectiveness



[6] Menéndez C, Bardají A, Sigauque B, Romagosa C, Sanz S, et al. (2008) A Randomized Placebo-Controlled Trial of Intermittent Preventive Treatment in Pregnant Women in the Context of Insecticide Treated Nets Delivered through the Antenatal Clinic. PLoS ONE 3(4): e1934. doi:10.1371/journal.pone.0001934.

[7] World Malaria Report 2012.

[8] DALYs = Disability Adjusted Life Years. The sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability.

[9] Net intervention costs for 1000 pregnant women were 13.15US$ (i.e. the difference between intervention costs and health cost for the treatment of malaria episodes averted).

[10] 11 times in the case of maternal malaria and 183 times in the case of neonatal mortality.

[11] Based on previous World Bank definitions Incremental cost-effectiveness ratios used to define the intervention as cost-effective were 129 US$ per DALY averted and 36 US$ per DALY averted to define the intervention as highly cost-effective.