

RBM WG MIP Annual Meeting

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ASPIRE

Aiming for Safe Pregnancies

Reducing Malaria and Infections of the Reproductive Tract

Matthew Chico

Assistant Professor

London School of Hygiene & Tropical Medicine

Email: matthew.chico@lshtm.ac.uk

Mobile: +44 794 844 4456 | Office: +44 207 927 2841

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IPTp-SP versus IPTp-DP

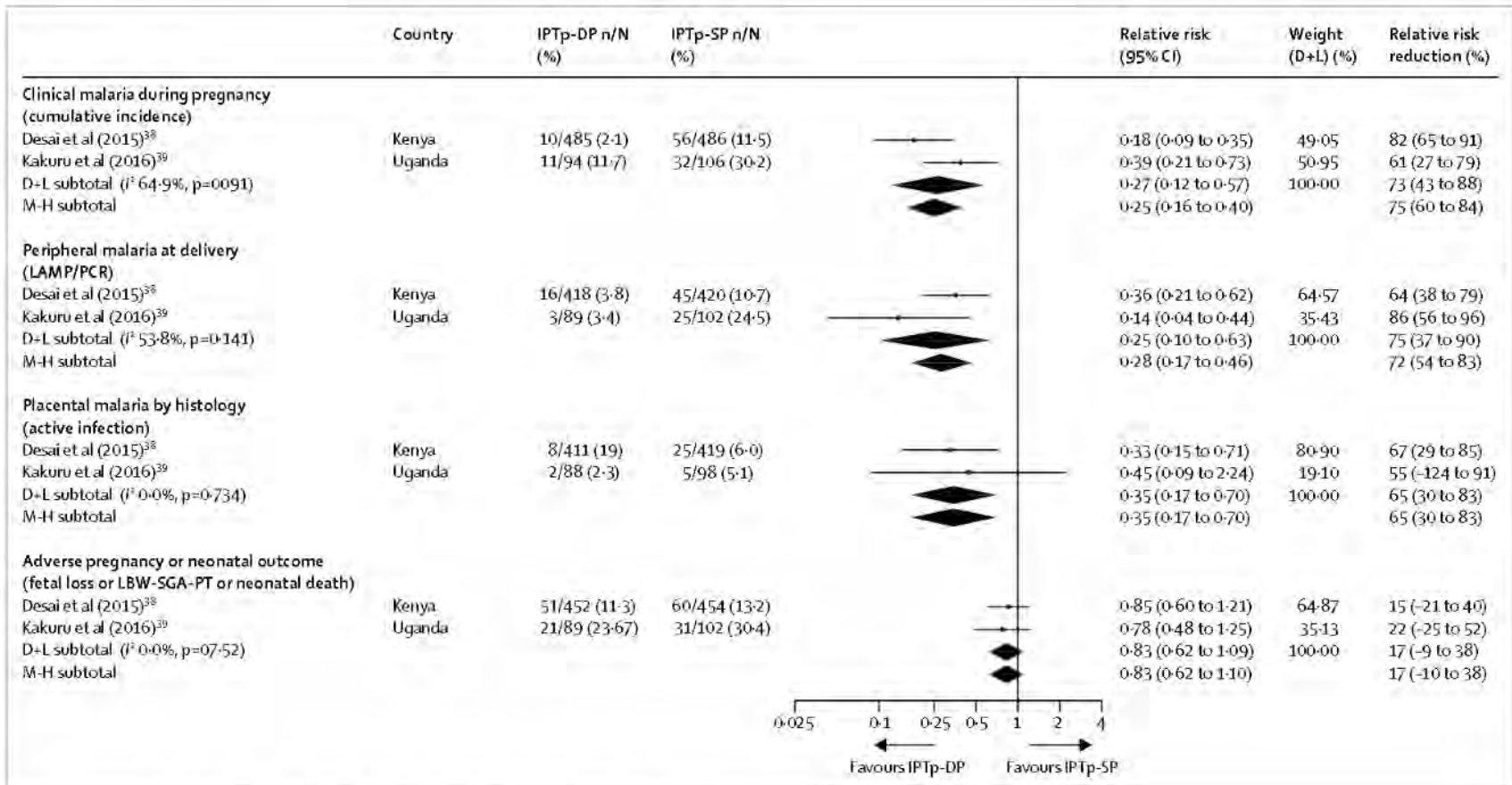


Figure 2: Forest plot of the efficacy of IPTp-DP vs IPTp-SP for the prevention of malaria in pregnancy in sub-Saharan Africa

Desai, Meghna, et al. "Prevention of malaria in pregnancy." *The Lancet infectious diseases* (2018).



Sulphonamide and STIs/RTIs



Sexually Transmitted Diseases
JOURNAL OF THE AMERICAN SEXUALLY TRANSMITTED DISEASES ASSOCIATION

Articles & Issues ▾ Collections For Authors ▾ Journal Info ▾

Introduction of Sulfonamide Therapy for Gonorrhea.
KAMPMEIER, R. H. MD
Sexually Transmitted Diseases: April/June 1983 - Volume 10 - Issue 2 - ppg 81-84

Sulphonamide curative of *Gonorrhoea*

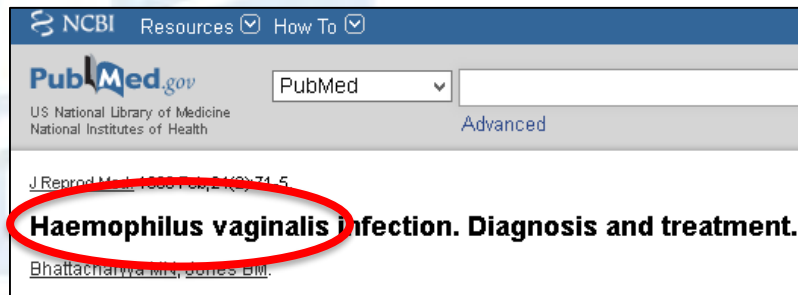


American Journal of Obstetrics and Gynecology
ELSEVIER Volume 142, Issue 2, 15 January 1982, Pages 125-129

GYNECOLOGY
Efficacy of treatment regimens for lower urogenital *Chlamydia trachomatis* infection in women

W.R. Bowie M.D., F.R.C.P.(C.)², L.M. Manzon BSN, C.J. Borrie-Hume BSN, M.P.H., A. Fawcett B.Sc., H.D. Jones M.D.

Sulphisoxazole curative of *chlamydia*



NCBI Resources [x] How To [x]

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed [v] [] Advanced

J Reprod Med. 1986 Feb; 21(2):71-5.
Haemophilus vaginalis infection. Diagnosis and treatment.
Bhattacharya M, Jones BM.

Sulphonamide curative of *Gardnerella vaginalis* (common BV-associated bacteria)



American Journal of Obstetrics and Gynecology
ELSEVIER Volume 50, Issue 3, September 1945, Pages 336-338

The Treatment of *Trichomonas Vaginitis* with a Sulfonamide Compound

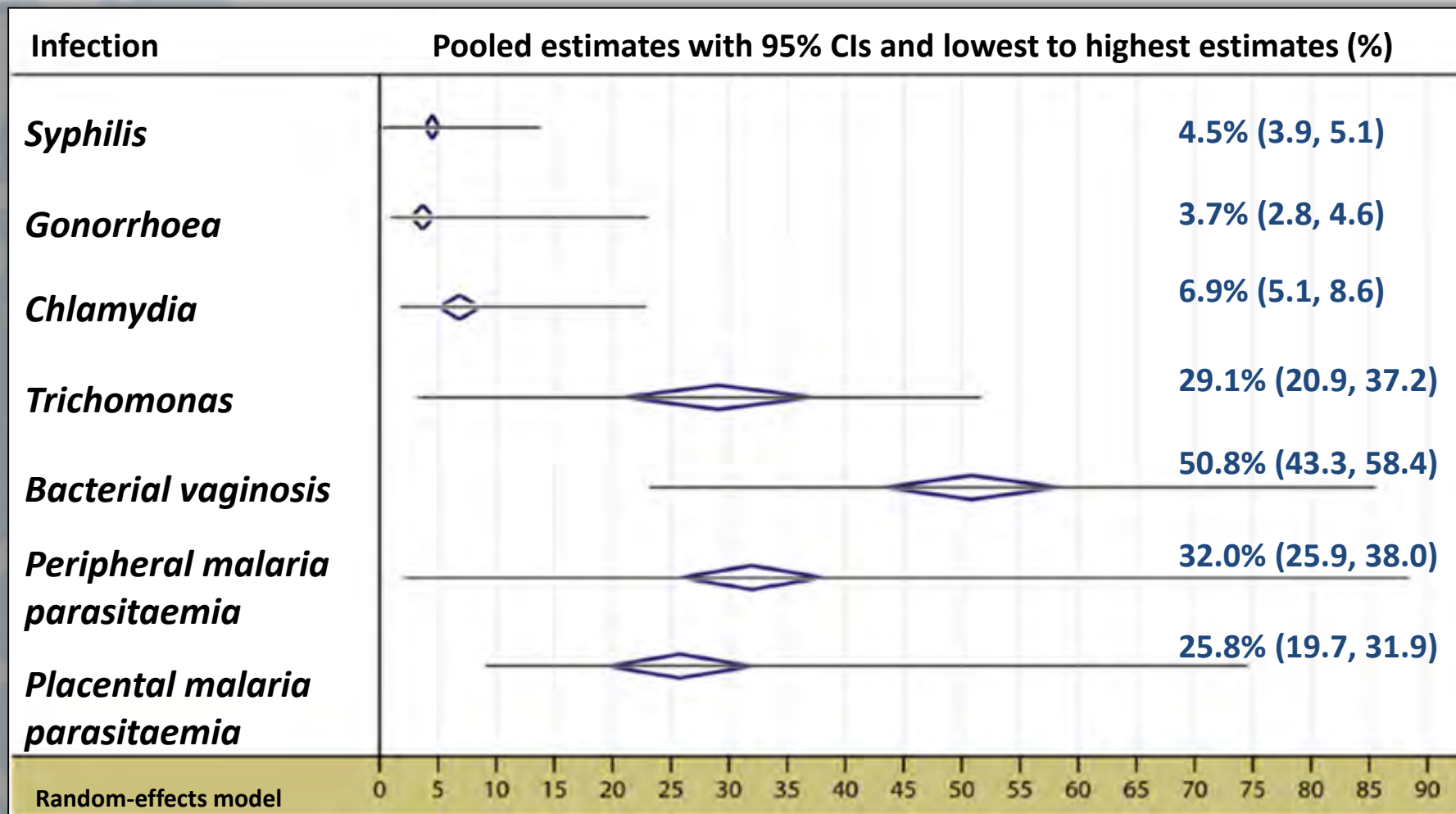
Helen M. Angelucci M.D., P.A.C.S.

Sulphonamide curative of trichomonas

Burden of malaria and curable STIs/RTIs in pregnancy

East and Southern Africa

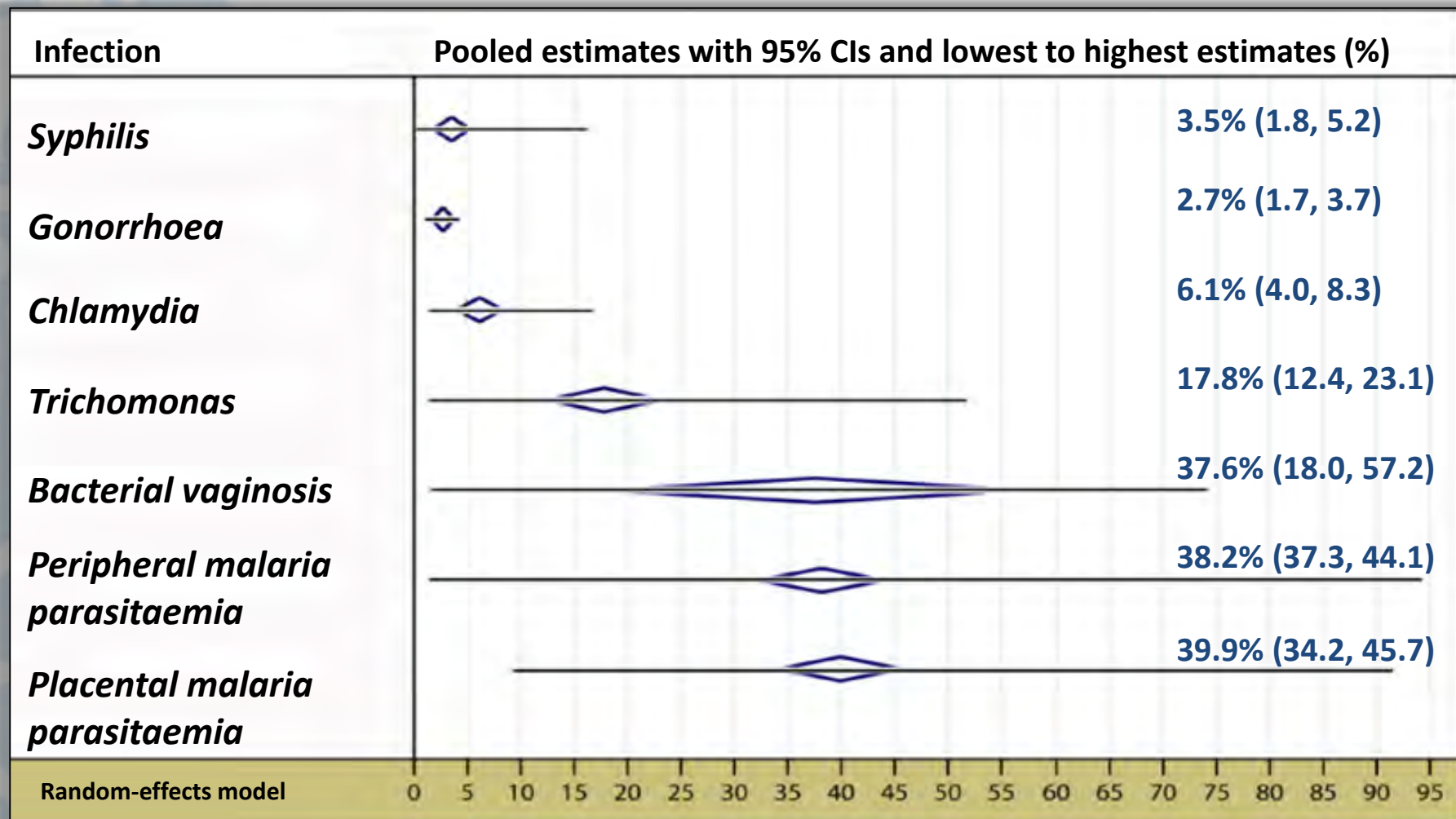
Pooled prevalence of malaria and STIs/RTIs in pregnancy with highest and lowest point estimates



Burden of malaria and curable STIs/RTIs in pregnancy

West and Central Africa

Pooled prevalence of malaria and STIs/RTIs in pregnancy with highest and lowest point estimates



Chico RM, Mayaud P, Ariti C, Mabey D, Ronsmans C, Chandramohan D. Prevalence of Malaria and Sexually Transmitted and Reproductive Tract Infections in Pregnancy in Sub-Saharan Africa: A Systematic Review. *JAMA*. May 16 2012;307(19):2079-2086.

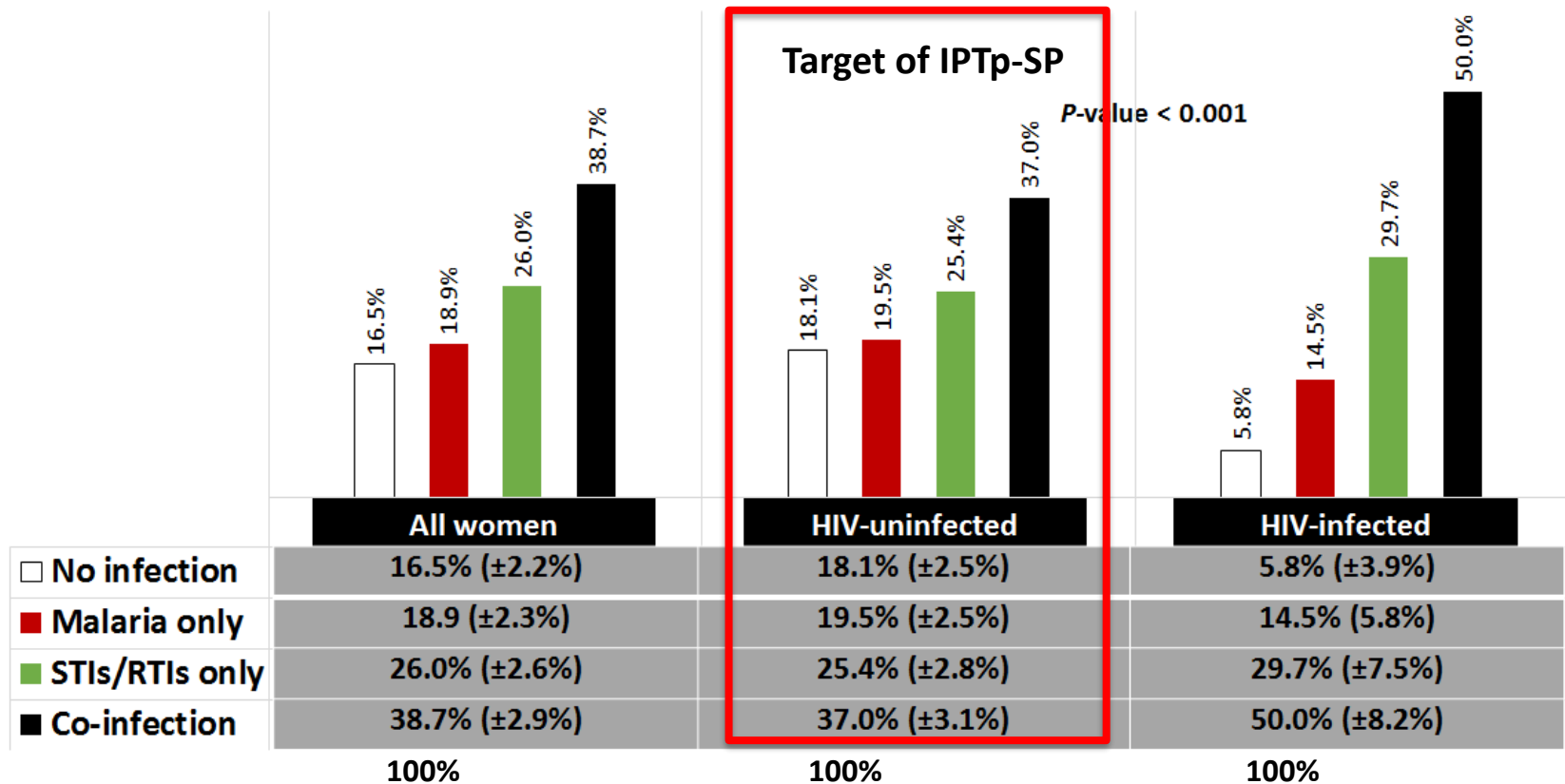
Leading candidates to replace SP

Option 1: Dihydroartemisinin-piperaquine (DP) alone

Option 2: Combination therapy that is protective against 'malaria and curable STIs/RTIs', eg.

1. DP plus azithromycin (Kenya, Tanzania, Malawi)
2. Piperaquine plus azithromycin (PNG)
3. SP plus metronidazole (Zambia)
4. DP plus metronidazole (Zambia)

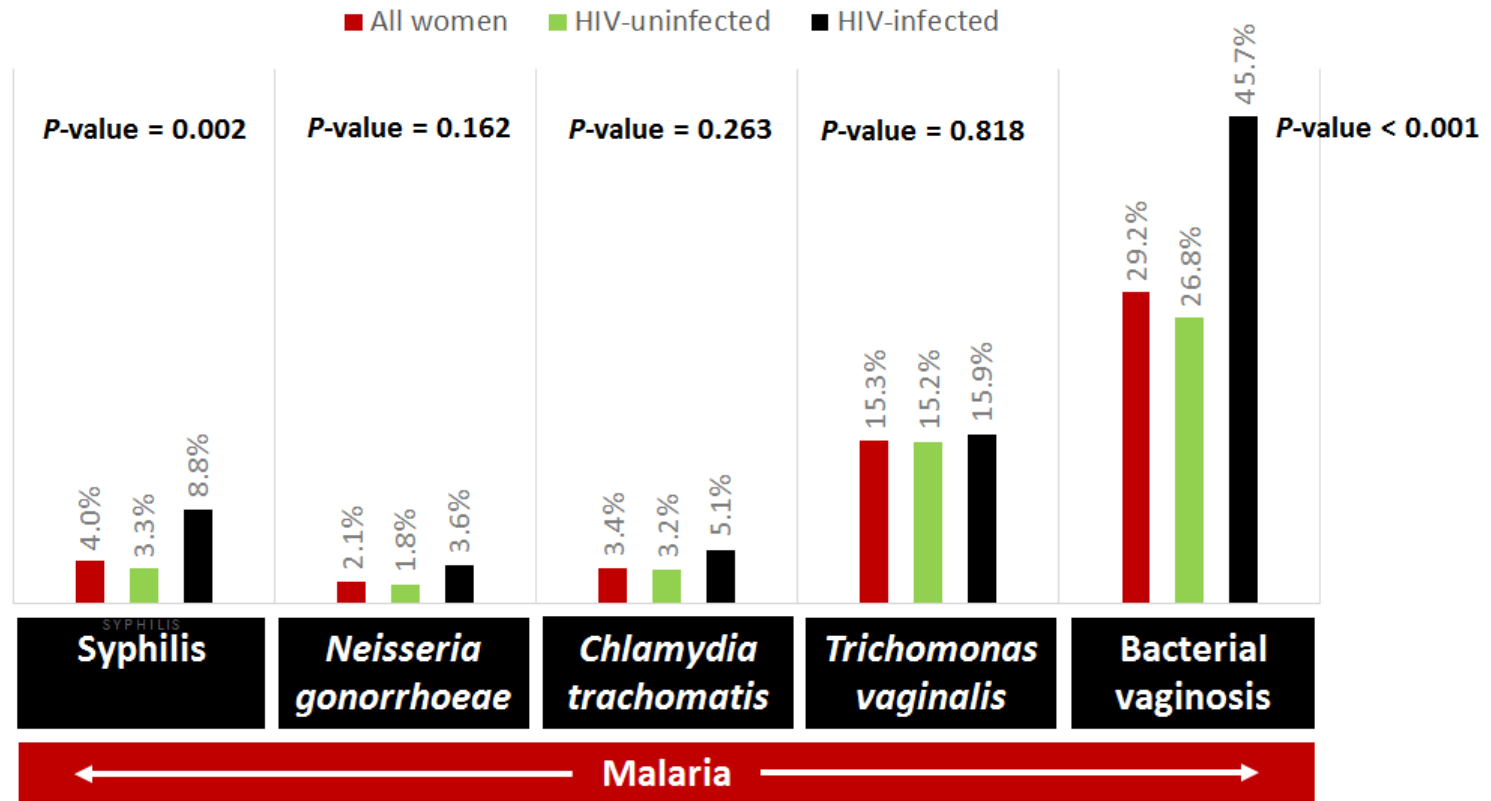
Prevalence of PCR-diagnosed malaria and any curable STI/RTI co-infection among pregnant women at antenatal care facilities in Nchelenge District, Zambia (2013-14)



Chaponda EB, Chico RM, Bruce J, et al. Malarial Infection and Curable Sexually Transmitted and Reproductive Tract Infections among Pregnant Women in a Rural District of Zambia. *American Journal of Tropical Medicine and Hygiene*, Volume 95, Issue 5, Nov 2016, pp. 1069-1076



Prevalence of PCR-diagnosed malaria and individual curable STIs/RTIs among pregnant women at antenatal care facilities in Nchelenge District, Zambia (2013-14)



Chaponda EB, Chico RM, Bruce J, et al. Malarial Infection and Curable Sexually Transmitted and Reproductive Tract Infections among Pregnant Women in a Rural District of Zambia. *American Journal of Tropical Medicine and Hygiene*, Volume 95, Issue 5, Nov 2016, pp. 1069-1076



IPTp-SP: malaria and non-malarial effects

Categories of maternal infection and exposure to doses 0 – 1 versus ≥ 2 doses of IPTp-SP among women with adverse birth outcomes

Adverse birth outcomes	0-1 dose IPTp-SP		≥ 2 doses IPTp-SP		Crude OR	95% CI	Adjusted OR	95% CI
	No. women	No. outcomes	No. women	No. outcomes				
Any adverse outcome								
<i>Malaria only</i>	20	13	129	41	0.25	0.09, 0.88	0.24	0.09, 0.66
<i>NG and/or CT only</i>	6	4	14	2	0.08	0.01, 0.80	0.08	0.01, 0.64
<i>No identified infection</i>	26	12	97	22	0.34	0.14, 0.85	0.27	0.11, 0.68
Low birth weight								
<i>No identified infection</i>	26	8	97	13	0.35	0.13, 0.96	0.24	0.08, 0.68
Preterm delivery								
<i>Malaria only</i>	20	10	129	21	0.19	0.07, 0.53	0.19	0.07, 0.53
<i>Malaria and TV and/or BV</i>	38	14	182	37	0.44	0.21, 0.93	0.45	0.21, 0.97
<i>NG and/or CT only</i>	6	4	14	2	0.08	0.01, 0.80	0.07	0.01, 0.73
<i>No identified infection</i>	26	10	97	12	0.23	0.08, 0.61	0.20	0.07, 0.54

NG = *Neisseria gonorrhoeae*; CT = *Chlamydia trachomatis*; TV = *Trichomonas vaginalis*; BV = Bacterial vaginosis

Chico RM, Chaponda EB, Ariti C, Chandramohan D. Sulfadoxine-pyrimethamine exhibits dose-response protection against adverse birth outcomes related to sexually transmitted and reproductive tract infections. *Clinical Infectious Diseases* (2 March, 2017) <https://doi.org/10.1093/cid/cix026>

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Study Interventions

5,436 pregnant women (1,812 per group)

Group 1: IPTp-SP* plus metronidazole (MTZ) placebo

Group 2: IPTp-SP plus MTZ*

Group 3: IPTp-DP plus MTZ*

* Baxy Pharmaceuticals of Ndola, Zambia
samples quality tested in LSHTM laboratories

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Study Population

HIV-negative pregnant women (all gravidae) between 16-28 weeks gestation assessed by ultrasound dating who have not yet started IPTp during the current pregnancy.

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Primary outcome

Any adverse pregnancy outcome

Composite of foetal loss (spontaneous abortion or stillbirth), or singleton live births born small for gestational age (SGA), or low birth weight (LBW; <2.5kg), or preterm delivery (<37 weeks), or neonatal death

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Secondary outcomes

- (1) single outcomes of the composite pregnancy outcome
- (2) incidence of clinical malaria
- (3) incidence of curable STIs/RTIs

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Sub-studies

Sub-study 1: *Effect of treatment on vaginal and intestinal microbiome and maternal cytokines* (London, UK)

Objective: To characterise the effect of treatment across trial arms on the vaginal and intestinal microbiota communities, vaginal and intestinal bacterial loads and soluble markers of inflammation.

Sub-studies

Sub-study 2: *In vitro testing of sulphadoxine and other antimicrobial agents* (Ndola, Zambia)

Objective: To measure the drug sensitivity of several pathogens implicated with WHO syndromes of vaginal discharge, lower abdominal pain, or genital ulcers in the presence of sulphadoxine and other antimicrobial agents.

Gantt chart



Activity	Pre-award	Year 1		Year 2		Year 3		Year 4	
		Prep	Recruitment and follow-up					Close	
Engage local, national and int'l stakeholders									
Prepare protocol and related documents									
Obtain ethics and regulatory approval									
Develop electronic data capture system									
Convene DMEC and TSC									
Deliver investigational products									
Conduct SOP and GCP training / review									
Enrol and follow-up participants									
Conduct trial audit or monitoring visit									
Conduct interim analysis									
End-line data analysis									



Investigators

Chief Investigators

- *Matthew Chico*
- *Daniel Chandramohan*

Local Principal Investigator - Zambia

- *Mike Chaponda*

Co-Investigators – Zambia

- *Modest Mulenga*
- *Sebastian Hachizovu*
- *Enesia Banda Chaponda Ngulube*

Co-Investigators – United Kingdom

- *Elizabeth Allen*
- *Philippe Mayaud*
- *Suzanna Francis*
- *Nigel Klein*
- *David MacIntyre*
- *Antonieta Medina-Lara*



Thanks to...

