

Arterolane-Piperaquine for the Treatment of Falciparum Malaria: A Meta-analysis of Randomized Controlled Trials

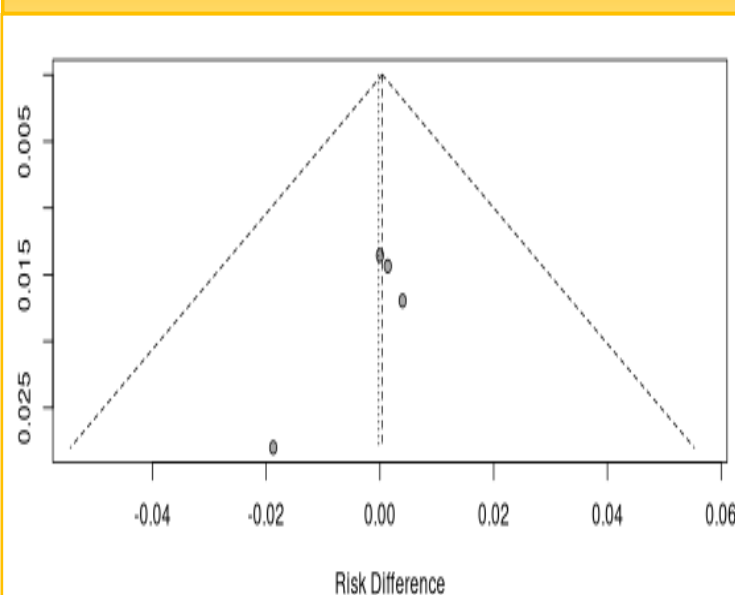
Background

Artemisinin combination therapy (ACT) resistance in falciparum malaria has emerged and is spreading. Newer antimalarials are needed to treat falciparum malaria cases. Arterolane maleate is a fully synthetic trioxolane antimalarial and active against *Plasmodium falciparum* malaria.

Methods

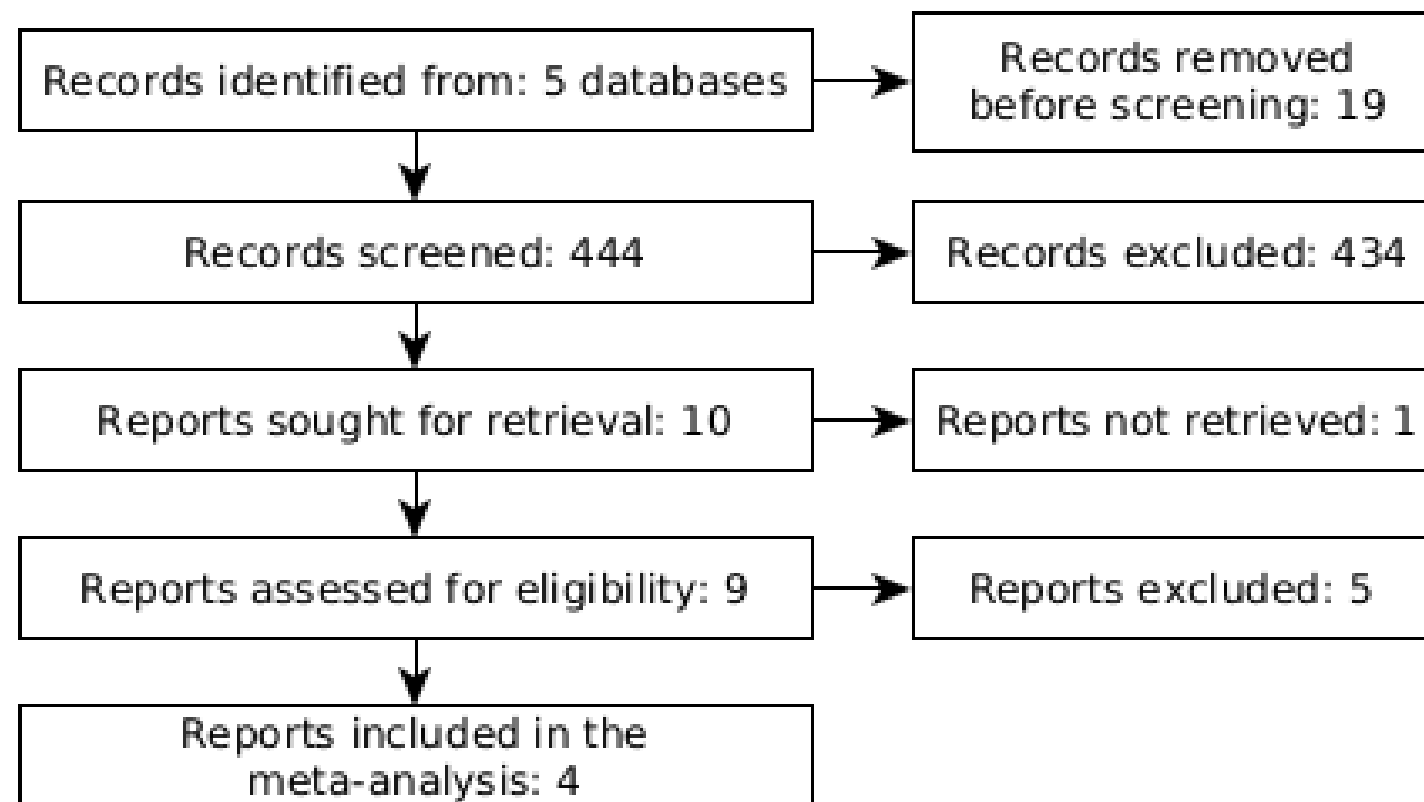
We conducted a meta-analysis to determine the safety and efficacy of arterolane maleate and piperaquine combination therapy for the treatment of uncomplicated falciparum malaria. We searched PubMed/MEDLINE, Cochrane Library, Google Scholar, ClinicalTrials.gov and MedRxiv using the search term “arterolane AND piperaquine AND falciparum”. Three authors conducted the search and screened the results by title, abstract and full text. Data extraction was done and analysis was performed using R version 4.2.0. Risk of bias analysis was done using Cochrane Risk of Bias tool version 2. The non-inferiority margin was set at 7%.

Funnel Plot

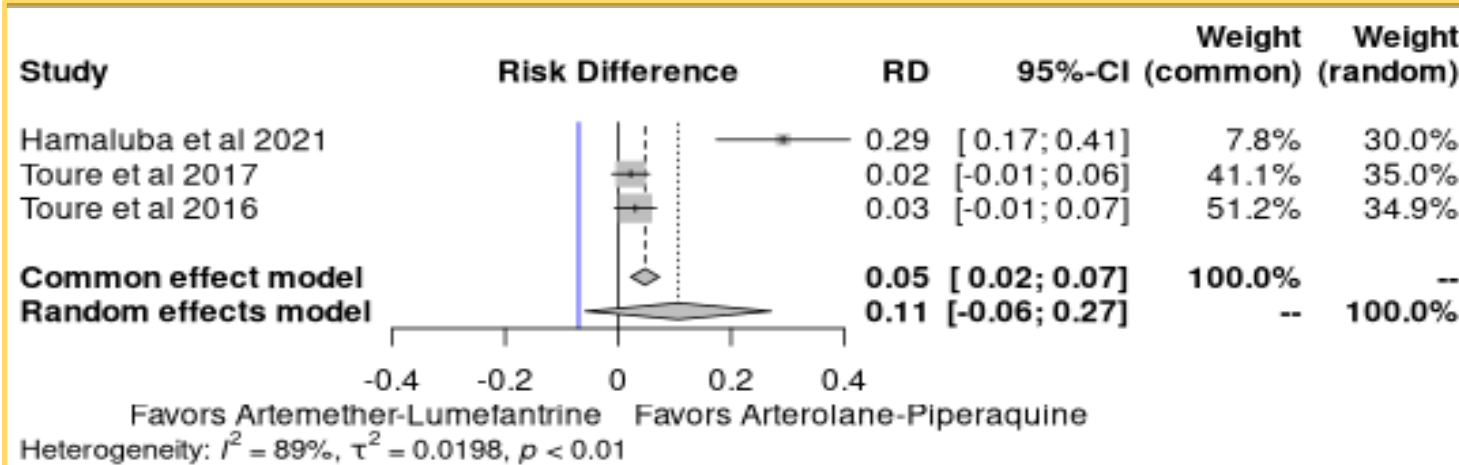


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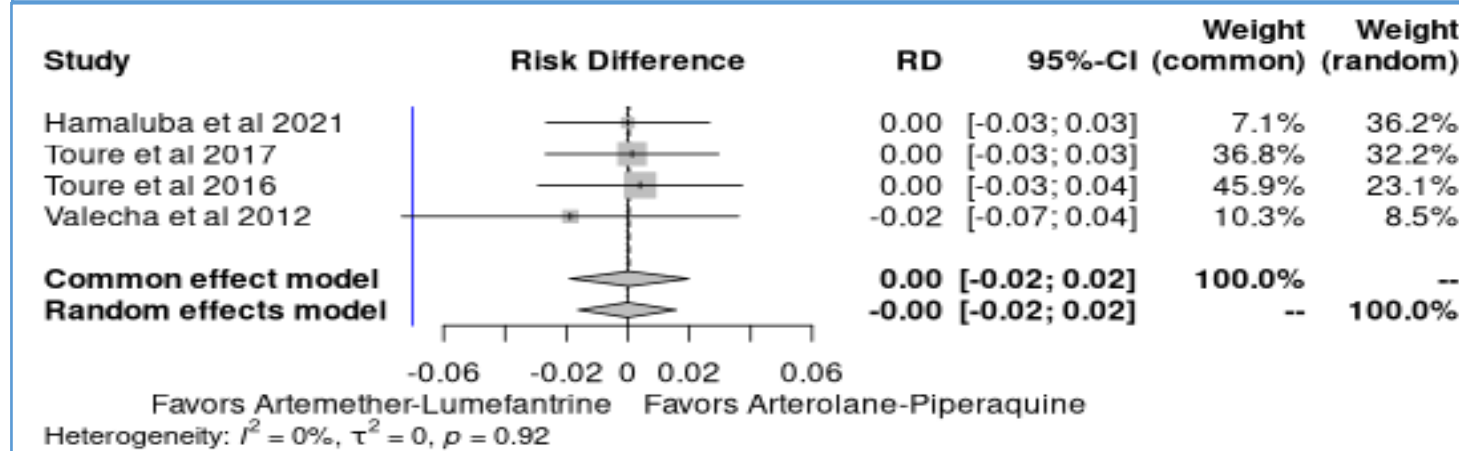
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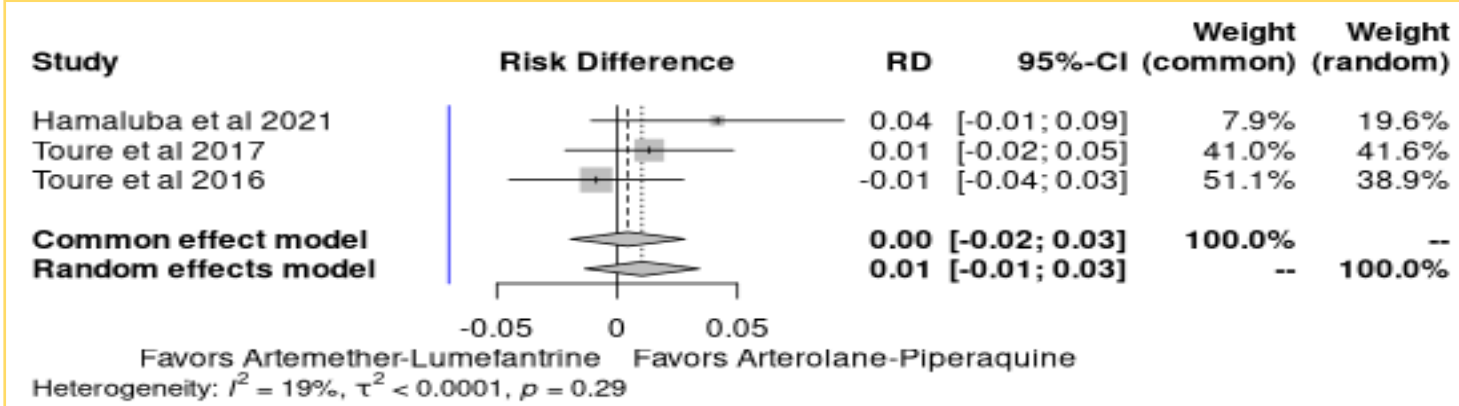
28 day PCR Uncorrected Risk Difference



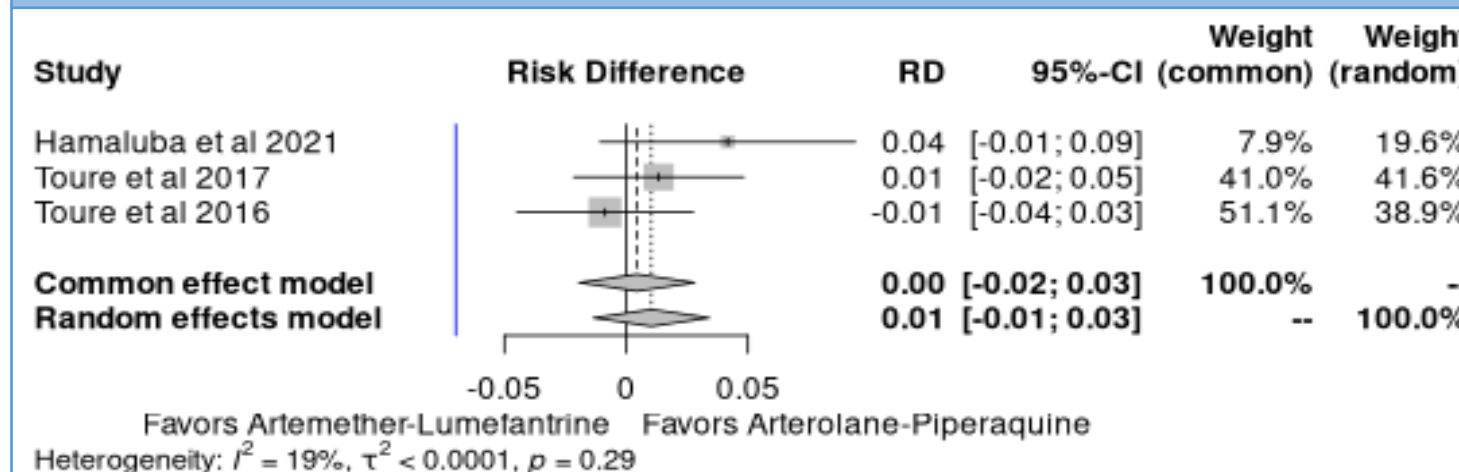
28 day PCR Corrected Risk Difference



42 day PCR Uncorrected Risk Difference



42 day PCR Corrected Risk Difference



Results

Four studies^{1,2,3,4} were included in the meta-analysis. Three studies had low risk of bias while one had high risk of bias. Using the fixed effect model, the 28 days Polymerase Chain Reaction (PCR) corrected risk difference between the artemether-lumefantrine and arterolane-piperaquine was **0 (95% confidence interval -0.02 to 0.02)** whereas PCR uncorrected risk difference was **0.05 (95% confidence interval 0.02 to 0.07)**. On 42 days follow-up the PCR uncorrected risk difference was **0.09 (95% confidence interval 0.06 to 0.12)** while the PCR corrected risk difference was **0 (95% confidence interval -0.02 to 0.03)**. Adverse effect profile was similar with risk difference of at least one adverse effect being **-0.01 (95% confidence interval -0.04 to 0.00)**.

Study Risk of Bias

Study	Risk of Bias
Hamaluba et al 2021	Low
Toure et al 2017	Low
Toure et al 2016	Low
Valecha et al 2012	High

Conclusion

Arterolane-piperaquine was non-inferior to artemether-lumefantrine for the treatment of uncomplicated falciparum malaria.

1. Hamaluba M et al. Arterolane-piperaquine-mefloquine versus arterolane-piperaquine and artemether-lumefantrine in the treatment of uncomplicated Plasmodium falciparum malaria in Kenyan children: a single-centre, open-label, randomised, non-inferiority trial. *Lancet Infect Dis*. 2021 Jun 7;
2. Toure OA et al. Assessment of Efficacy and Safety of Arterolane Maleate-Piperaquine Phosphate Dispersible Tablets in Comparison With Artemether-Lumefantrine Dispersible Tablets in Pediatric Patients With Acute Uncomplicated Plasmodium falciparum Malaria: A Phase 3, Randomized, Multicenter Trial in India and Africa. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2017 Oct 30;65(10):1711–20.
3. Toure OA et al. A Phase 3, Double-Blind, Randomized Study of Arterolane Maleate-Piperaquine Phosphate vs Artemether-Lumefantrine for Falciparum Malaria in Adolescent and Adult Patients in Asia and Africa. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2016 Apr 15;62(8):964–71.
4. Valecha N et al. Arterolane maleate plus piperaquine phosphate for treatment of uncomplicated Plasmodium falciparum malaria: a comparative, multicenter, randomized clinical trial. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2012 Sep;55(5):663–71