

Annals of Infectious Diseases and Therapy

Review Article

Clinical Outcomes of combination antibiotic therapy in Patients with malaria

Ferrari G^{1*}, Russo D² and Bruno M³

¹Department of Clinical Vaccinology, Parana Academy of Vaccinology, Portugal

²Department of Infectious Diseases, Lena Institute for Advanced Vaccinology, Spain

³Department of Epidemiology, Orinoco Research Center for Epidemiology, Greece

*Address for Correspondence: Giulia Ferrari, Department of Clinical Vaccinology, Parana Academy of Vaccinology, Portugal; E-mail: giulia.ferrari@parana.edu

Received: 20 April 2025; Accepted: 10 July 2025; Published: 28 September 2025.

Citation of this article: Ferrari G, Russo D, Bruno M (2025) Clinical Outcomes of combination antibiotic therapy in Patients with malaria. Ann Infect Dis Ther, 6(1): 01-06. DOI: [10.5281/zenodo.22811748](https://doi.org/10.5281/zenodo.22811748)

Copyright: © 2025 Giulia Ferrari, et al. This is an open access article distributed under the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Background: Combination therapy is now standard across malaria care: artemisinin-based combinations for falciparum malaria, and, where bacterial infection coexists, combined antimalarial-antibacterial regimens [2,20].

Objective: This review synthesizes outcomes for combination antimalarial therapy in uncomplicated and severe malaria, resistance's impact on that strategy, and combined antimalarial-antibacterial therapy in bacterial co-infection.

Methods: We synthesized trials and meta-analyses of artemisinin combinations, resistance-surveillance studies, and cohorts and trials on bacterial co-infection and antibacterial therapy in malaria patients.

Findings: Artesunate combinations roughly halve treatment failure in uncomplicated malaria [7]; intravenous artesunate lowers severe-malaria mortality versus quinine, from 22% to 15% in adults and roughly 10.9% to 8.5% in children [10,11]; triple combinations extend this where resistance has emerged [18]; and bacterial co-infection, in roughly 6% of severe-malaria children, more than doubles case fatality (24.1% vs 10.2%) despite imprecise clinical criteria for antibacterial cover [20,6].

Conclusions: Combination therapy improves malaria outcomes through distinct mechanisms by scenario; sustained resistance surveillance and better diagnostics for antibacterial targeting will determine whether that benefit holds [16,20].

Keywords: malaria; artemisinin-based combination therapy; antibiotic co-therapy; bacteremia; drug resistance

1. Introduction

Malaria treatment has been built on combination therapy for two decades now, though not for the reason combination therapy is usually invoked in infectious disease. Where combining antimicrobials against tuberculosis or HIV is primarily about preventing resistance to a single drug, the case for artemisinin-based combination therapy (ACT) in falciparum malaria rests almost as much on pharmacodynamics: an artemisinin clears most of the parasite biomass within 24 to 48 hours, and a longer-acting partner drug is needed to mop up the residual parasites its short half-life cannot reach before elimination [1]. Kremsner and Krishna's review of antimalarial combinations laid out this logic, arguing that pairing a fast, rapidly eliminated artemisinin with a slower partner both hastens cure and protects the partner from the resistance monotherapy would otherwise invite [2]. The scale of the problem is not small: Snow and colleagues' global mapping estimated several hundred million clinical episodes of falciparum malaria annually, concentrated in sub-Saharan Africa, a burden that gives even a modest gain in cure rate or mortality real population-level weight [3]. White and colleagues' clinical seminar situates that burden across the full disease spectrum, from asymptomatic parasitemia to the multi-organ dysfunction of severe disease, and it is across that spectrum that the combination-therapy questions here play out differently by patient [4].

This review uses "combination antibiotic therapy in patients with malaria" in the sense the phrase actually needs in this disease: the artemisinin combinations now first-line for uncomplicated and severe falciparum malaria, and the antibacterial regimens frequently, and sometimes necessarily, layered onto antimalarial treatment when a patient also carries a bacterial infection. Malaria and bacteremia are not mutually exclusive diagnoses, and a nontrivial fraction of patients, especially severely ill children in high-transmission settings, present with both at once, an overlap that has shaped empirical

antibiotic guidance in malaria-endemic settings for years [5,6]. We synthesize evidence on three connected questions: what outcomes combination antimalarial therapy achieves in uncomplicated and severe malaria, how antimalarial resistance has pushed combination strategy further, and what is known about combining antibacterial and antimalarial treatment in patients with bacterial co-infection.

2. Methods

This is a narrative synthesis rather than a systematic review. We drew on randomized controlled trials of artemisinin-based combinations in uncomplicated and severe malaria, the meta-analyses and Cochrane reviews pooling those trials, the surveillance literature documenting artemisinin resistance, and the observational and trial literature on bacterial co-infection and antibacterial therapy in malaria patients. Studies were chosen to represent the major treatment eras, from quinine monotherapy through first-generation ACTs to the triple-combination regimens now being trialed against partial artemisinin resistance, and the geographic range, principally sub-Saharan Africa and the Greater Mekong subregion, where transmission intensity and resistance prevalence differ substantially. Table 1 first situates the major regimens against one another before the results turn to the trial evidence and the bacterial co-infection literature.

3. Results

Efficacy of artemisinin-based combinations in uncomplicated malaria

The core clinical case for combination over monotherapy in uncomplicated falciparum malaria was established by Adjuik and colleagues' individual-patient meta-analysis of more than a dozen trials, which found that adding a three-day course of artesunate to a partner antimalarial reduced treatment failure by roughly half and substantially reduced gametocyte carriage, the transmission stage of the parasite [7]. Nosten and White's

synthesis of the ACT evidence base placed this gain in context, tracing the shift from chloroquine and sulfadoxine-pyrimethamine monotherapy, both of which had by the 1990s lost efficacy across large parts of Africa and Southeast Asia, to artemether-lumefantrine, artesunate-amodiaquine, artesunate-mefloquine and dihydroartemisinin-piperaquine as the regimens that came to dominate national guidelines [8]. Guerin and colleagues' broader appraisal of malaria control argued that this shift was not an incremental refinement but a necessary response to a genuine crisis in monotherapy efficacy, requiring investment in new fixed-dose formulations as much as in the underlying pharmacology [9].

Table 1: Major parenteral and oral antimalarial combination regimens discussed in this review, by treatment era and principal clinical role [2,8,10,11,18].			
Regimen	Backbone / partner	Principal indication	Clinical role
Quinine monotherapy	Quinine	Severe malaria (historical standard)	Superseded parenteral backbone; higher mortality than artesunate
Intravenous artesunate	Artesunate alone, then oral ACT	Severe malaria	First-line parenteral backbone; lower mortality than quinine
Artemether-lu mefantrine / ar tesunate-amod iaquine	Artemisinin + partner drug	Uncomplicated malaria	Standard first-line ACT
Dihydroartemi sinin-piperaqui ne	Artemisinin + piperaquine	Uncomplicated malaria	Standard first-line ACT, longer partner half-life
Triple ACT (ACT + second partner drug)	Artemisinin + two partner drugs	Uncomplicated malaria with partner-drug resistance	Investigational extension of the combination principle

Severe malaria: combination parenteral therapy and mortality

The clearest outcome data for combination antimalarial strategy come from severe malaria, where the choice of parenteral backbone, before any oral partner drug follows, has been shown directly to change mortality. The

Southeast Asian Quinine Artesunate Malaria Trial randomized patients with severe falciparum malaria to intravenous artesunate or quinine and found mortality of 15% with artesunate against 22% with quinine, a relative risk of 0.69 translating to roughly one death averted per 11 to 20 patients treated [10]. The subsequent AQUAMAT trial extended this comparison to African children, who bear most of the world's severe malaria mortality, and again found lower mortality with artesunate, at roughly 8.5% against 10.9%, confirming the benefit generalized to the population where severe malaria is most common [11] (Figure 1). Sinclair and colleagues' Cochrane review, pooling these and other trials, concluded artesunate should replace quinine as the treatment of choice for severe falciparum malaria in adults and children alike, a recommendation most national and WHO guidelines have since adopted [12]. Achan and colleagues' review of quinine's continuing role reinforces why this matters clinically: quinine remains an essential fallback where artesunate is unavailable or in early pregnancy, but its narrower therapeutic margin and now inferior mortality outcome have displaced it from first-line status wherever artesunate can be supplied [13].

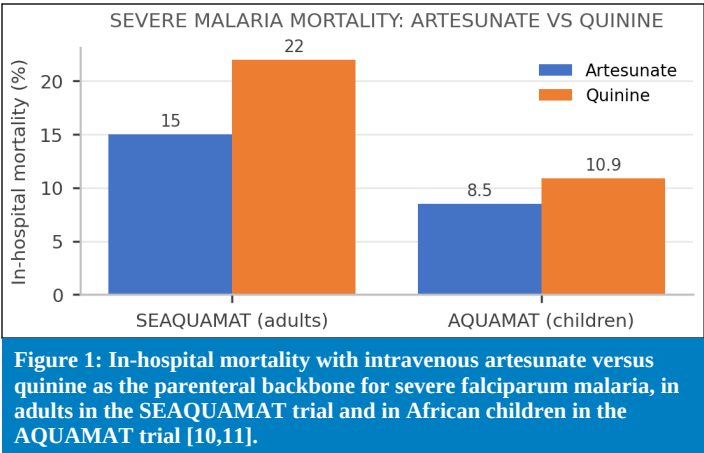


Figure 1: In-hospital mortality with intravenous artesunate versus quinine as the parenteral backbone for severe falciparum malaria, in adults in the SEAQUAMAT trial and in African children in the AQUAMAT trial [10,11].

Artemisinin resistance and the push toward triple combinations

The combination strategy built around artemisinins has itself come under threat from resistance, driving the

search for further combination refinement. Noedl and colleagues first documented delayed parasite clearance consistent with reduced artemisinin susceptibility in western Cambodia [14], and Dondorp and colleagues' subsequent characterization confirmed unambiguous resistance at the Thailand-Cambodia border, manifesting as markedly slower clearance rather than outright treatment failure, since the ACT partner drug could still, for a time, clear the residual burden left behind [15]. Ashley and colleagues' multicountry surveillance mapped the subsequent spread across the Greater Mekong subregion, and Tun and colleagues' K13 molecular marker survey documented its arrival in Myanmar, closing much of the gap toward the Indian subcontinent that had offered some reassurance [16,17]. The clinical concern is direct: as clearance slows, the partner drug must control a larger residual parasite population for longer, eroding the protection the combination was designed to provide. Van der Pluijm and colleagues' multicentre randomized trial of triple artemisinin-based combinations, adding a second unrelated partner drug to standard ACT, found the triple regimens outperformed standard two-drug ACT specifically where partner-drug resistance was already established, evidence that extending, rather than abandoning, the combination principle remains the most deployable response to a resistant parasite [18].

Bacterial co-infection and adjunctive antibacterial therapy

A materially different combination question arises when the patient has malaria and a bacterial infection at the same time, common enough in high-transmission settings that WHO guidance has long recommended empirical antibacterial cover for children with severe malaria and features suggestive of sepsis. Berkley and colleagues' prospective study of bloodstream infection among children admitted to a rural Kenyan hospital found substantial bacteremia prevalence among febrile admissions and a strong association with mortality, establishing malaria and bacterial infection as frequently

co-occurring rather than mutually exclusive diagnoses [5]. Scott and colleagues' case-control and longitudinal study in the same region found that recent or concurrent parasitemia was itself associated with increased bacteremia risk, particularly nontyphoidal *Salmonella*, consistent with malaria-induced immune and splenic dysfunction transiently raising vulnerability to invasive bacterial disease [19]. Church and Maitland's systematic review put a number on the overlap: invasive bacterial co-infection occurred in roughly 6.4% of children with severe malaria and 5.6% across all severities, and case fatality among children with both malaria and confirmed co-infection reached 24.1%, more than double the 10.2% among malaria alone [20] (Figure 2). Bronzan and colleagues' Malawian cohort found a lower bacteremia prevalence of 4.6% overall, rising to 11.7% in severe malarial anemia, the phenotype where bacteremia clusters most heavily [21]. Bassat and colleagues and Were and colleagues reported comparable patterns in Mozambican and Kenyan cohorts, confirming this is a general feature of pediatric severe malaria across sub-Saharan Africa [22,23].

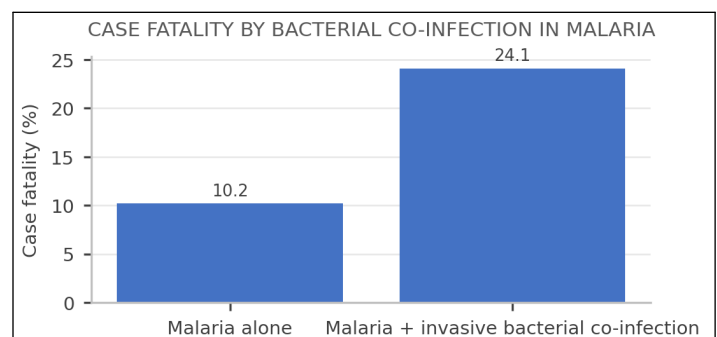


Figure 2: Case fatality among African children with malaria alone versus malaria with confirmed invasive bacterial co-infection (IBI), pooled across the pediatric cohorts synthesized in a systematic review [20].

Guideline-directed empirical antibacterial use and its trade-offs

Because clinical features alone distinguish severe malaria from severe bacterial sepsis poorly in a febrile, critically ill child, WHO guidelines have for years recommended

broad-spectrum antibacterial cover alongside antimalarial treatment for children with severe malaria and any feature suggestive of bacterial infection. Nadjm and colleagues' prospective evaluation of this guidance in a high-transmission area of Tanzania found that the WHO criteria identified most children who truly had invasive bacterial disease, but at a substantial cost in unnecessary exposure, since most children who met the criteria and received empirical antibiotics turned out, on culture, not to have bacteremia at all [6]. This is the trade-off combination antimalarial-plus-antibacterial therapy has to navigate: undertreating the bacteremic minority carries a case-fatality penalty Church and Maitland's pooled data show is severe, while treating every child who meets broad criteria exposes a much larger group to antibacterial therapy they do not need, with the attendant costs of toxicity, resource use, and resistance pressure. Maitland and colleagues' FEAST trial, conducted in the same population of severely unwell East African children with severe febrile illness including malaria, found that a bolus fluid strategy actually increased mortality, a reminder that interventions layered onto standard care in this population need direct trial evidence rather than physiological plausibility alone [24].

Table 2: Reported clinical outcomes associated with combination antimalarial and, where relevant, combined antimalarial-antibacterial therapy across the trials and cohorts synthesized in this review [10,11,20,21,26].			
Study / cohort	Population	Comparison	Reported outcome
[10] SEAQU AMAT	Adults, severe malaria, SE Asia	IV artesunate vs quinine	Mortality 15% vs 22% (RR 0.69)
[11] AQUAMAT	Children, severe malaria, Africa	IV artesunate vs quinine	Mortality approximately 8.5% vs 10.9%
[20]	African children, malaria +/- IBI	Malaria with vs without bacterial co-infection	Case fatality 24.1% vs 10.2%
[21]	Malawian children, severe malaria	Bacteremia prevalence by phenotype	4.6% overall; 11.7% in severe malarial anemia

Study / cohort	Population	Comparison	Reported outcome
[26]	Pregnant women, Africa	Azithromycin-chloroquine vs sulfadoxine-pyrimethamine	Broadly comparable efficacy against placental malaria

Antibiotic-antimalarial combinations for specific indications

A narrower but genuine example of an antibacterial deliberately paired with an antimalarial in the same regimen, rather than added empirically for suspected sepsis, is azithromycin alongside chloroquine or sulfadoxine-pyrimethamine for intermittent preventive treatment of malaria in pregnancy, chosen partly for its antimalarial contribution and partly for coverage of curable sexually transmitted and reproductive tract infections common in the same population. Chico and colleagues' early appraisal argued that azithromycin's activity against Chlamydia trachomatis, Neisseria gonorrhoeae and Treponema pallidum made it a rational partner where both malaria and untreated sexually transmitted infection contribute to adverse pregnancy outcomes [25]. Kimani and colleagues' open-label randomized trial compared azithromycin-chloroquine against standard sulfadoxine-pyrimethamine across multiple African sites and found broadly comparable efficacy against placental malaria and low birth weight, evidence that antibiotic-antimalarial combinations can be built for reasons beyond resistance prevention when disease burden genuinely overlaps [26].

4. Discussion

The evidence assembled here supports a layered rather than a single-mechanism view of what "combination therapy" means for clinical outcomes in malaria. At the level of the parasite itself, artemisinin-based combinations have delivered large, well-replicated gains: lower treatment failure and transmission potential in uncomplicated disease [7], and a mortality reduction in severe disease large enough to have changed global guidelines within a decade of the pivotal trials [10,11,12].

That gain is not permanent by default. Artemisinin resistance, first documented in western Cambodia and now confirmed across a widening area of the Greater Mekong subregion, has already begun eroding the pharmacodynamic assumption the strategy rests on, and the field's response, adding a third drug rather than abandoning the combination principle, is itself evidence for how much clinical value that principle still carries under partial resistance [14,16,17,18].

The second, clinically distinct, sense in which combination therapy matters in malaria is the frequent, biologically plausible overlap between falciparum infection and invasive bacterial disease, particularly in African children with severe anemia [19,21]. Here the evidence is less about a single intervention's efficacy than a genuinely difficult diagnostic and stewardship problem: Church and Maitland's pooled case-fatality gap between malaria with and without bacterial co-infection is large enough that undertreating it is clearly costly, and Nadjm and colleagues' Tanzanian data show that current WHO criteria catch most of that risk only by exposing a much larger group of culture-negative children to antibacterial therapy they did not need [20,6]. Resolving that trade-off will likely depend more on point-of-care diagnostics for invasive bacterial infection than on any refinement of the antimalarial regimen, since the two components of care here address genuinely separate pathogens rather than reinforcing a single mechanism as an ACT's two components do. The azithromycin-based regimens for intermittent preventive treatment of malaria in pregnancy occupy a middle position, deliberately built around two organisms rather than around resistance prevention or empirical sepsis cover, and Kimani and colleagues' trial data suggest a purpose-built dual-indication combination can match standard therapy on its primary endpoint while adding value against a second, coprevalent disease [25,26].

Taken together with the regimen comparison in Table 1

and the outcome data in Table 2, "combination therapy" in malaria is doing at least three different jobs at once: protecting a fast-acting drug from resistance, achieving a mortality benefit through a superior parenteral backbone, and, for bacterial co-infection, layering a second antimicrobial class onto antimalarial treatment to cover a genuinely separate pathogen. A clinician managing a malaria patient needs to recognize which of those problems is actually in front of them before treatment can be optimized.

5. Conclusion

Across three distinct clinical scenarios, uncomplicated falciparum malaria, severe malaria, and malaria complicated by bacterial co-infection, the outcome data consistently favor a combination approach over any single-agent alternative, though the mechanism differs across the three. Artemisinin-based combinations reduce treatment failure and transmission in uncomplicated disease [7] and reduce mortality directly when artesunate replaces quinine as the parenteral backbone in severe disease [10,11]; triple combinations now extend that protective logic where partner-drug resistance has begun eroding standard ACT efficacy [18]. Where malaria and invasive bacterial infection coincide, which pooled pediatric data suggest happens often enough, and with a severe enough case-fatality penalty, to demand attention, combination therapy spanning antimalarial and antibacterial classes remains necessary despite the diagnostic uncertainty and antibiotic overuse current clinical criteria still generate [20,6]. Continued benefit from all three strategies will depend on sustained resistance surveillance for the antimalarial component and better diagnostics to target the antibacterial component more precisely than current algorithms allow.

6. Acknowledgements

The authors thank colleagues at their respective institutions for helpful discussion during the preparation of this review.

7. Funding

This work received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

8. Conflict of Interest

The authors declare that they have no competing interests.

9. Author Contributions

All authors contributed to the conception of the review, literature synthesis, drafting and critical revision of the manuscript, and approved the final version for submission.

10. Ethics Statement

This article is a literature review and did not involve new data collection from human or animal subjects; no ethics approval was required.

11. Data Availability

No new data were generated for this review. All sources synthesized are cited in the reference list and are publicly available through their original publications.

12. References

1. White, N.J., Nosten, F., Looareesuwan, S., Watkins, W.M., Marsh, K., Snow, R.W., et al. (1999) Averting a malaria disaster. *Lancet*, 353(9164): 1965-1967.
2. Kremsner, P.G., Krishna, S. (2004) Antimalarial combinations. *Lancet*, 364(9430): 285-294. DOI: [10.1016/S0140-6736\(04\)16680-4](https://doi.org/10.1016/S0140-6736(04)16680-4)
3. Snow, R.W., Guerra, C.A., Noor, A.M., Myint, H.Y., Hay, S.I. (2005) The global distribution of clinical episodes of *Plasmodium falciparum* malaria. *Nature*, 434(7030): 214-217. DOI: [10.1038/nature03342](https://doi.org/10.1038/nature03342)
4. White, N.J., Pukrittayakamee, S., Hien, T.T., Faiz, M.A., Mokuolu, O.A., Dondorp, A.M. (2014) Malaria. *Lancet*, 383(9918): 723-735. DOI: [10.1016/S0140-6736\(13\)60024-0](https://doi.org/10.1016/S0140-6736(13)60024-0)
5. Berkley, J.A., Bejon, P., Mwangi, T., Gwer, S., Maitland, K., Williams, T.N., et al. (2005) Bacteremia among children admitted to a rural hospital in Kenya. *New England Journal of Medicine*, 352(1): 39-47. DOI: [10.1056/NEJMoa040275](https://doi.org/10.1056/NEJMoa040275)
6. Nadjm, B., Amos, B., Mtove, G., Ostermann, J., Chonya, S., Wangai, H., et al. (2010) WHO guidelines for antimicrobial treatment in children admitted to hospital in an area of intense *Plasmodium falciparum* transmission: prospective study. *BMJ*, 340: c1350. DOI: [10.1136/bmj.c1350](https://doi.org/10.1136/bmj.c1350)
7. Adjuik, M., Babiker, A., Garner, P., Olliaro, P., Taylor, W., White, N. (2004) Artesunate combinations for treatment of malaria: meta-analysis. *Lancet*, 363(9402): 9-17. DOI: [10.1016/S0140-6736\(03\)15162-8](https://doi.org/10.1016/S0140-6736(03)15162-8)
8. Nosten, F., White, N.J. (2007) Artemisinin-based combination treatment of falciparum malaria. *American Journal of Tropical Medicine and Hygiene*, 77(6 Suppl): 181-192.
9. Guerin, P.J., Olliaro, P., Nosten, F., Druilhe, P., Laxminarayan, R., Binka, F., et al. (2002) Malaria: current status of control, diagnosis, treatment, and a proposed agenda for research and development. *Lancet Infectious Diseases*, 2(9): 564-573. DOI: [10.1016/S1473-3099\(02\)00239-6](https://doi.org/10.1016/S1473-3099(02)00239-6)
10. Dondorp, A., Nosten, F., Stepniewska, K., Day, N., White, N. (2005) Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial. *Lancet*, 366(9487): 717-725. DOI: [10.1016/S0140-6736\(05\)67176-0](https://doi.org/10.1016/S0140-6736(05)67176-0)
11. Dondorp, A.M., Fanello, C.I., Hendriksen, I.C., Gomes, E., Seni, A., Chhaganlal, K.D., et al. (2010) Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. *Lancet*, 376(9753): 1647-1657. DOI: [10.1016/S0140-6736\(10\)61924-1](https://doi.org/10.1016/S0140-6736(10)61924-1)
12. Sinclair, D., Donegan, S., Isba, R., Laloo, D.G. (2012) Artesunate versus quinine for treating severe malaria. *Cochrane Database of Systematic Reviews*, 2012(6): CD005967. DOI: [10.1002/14651858.CD005967.pub4](https://doi.org/10.1002/14651858.CD005967.pub4)

13. Achan, J., Talisuna, A.O., Erhart, A., Yeka, A., Tibenderana, J.K., Baliraine, F.N., et al. (2011) Quinine, an old anti-malarial drug in a modern world: role in the treatment of malaria. *Malaria Journal*, 10: 144. DOI: [10.1186/1475-2875-10-144](https://doi.org/10.1186/1475-2875-10-144)
14. Noedl, H., Se, Y., Schaecher, K., Smith, B.L., Socheat, D., Fukuda, M.M. (2008) Evidence of artemisinin-resistant malaria in western Cambodia. *New England Journal of Medicine*, 359(24): 2619-2620. DOI: [10.1056/NEJMc0805011](https://doi.org/10.1056/NEJMc0805011)
15. Dondorp, A.M., Nosten, F., Yi, P., Das, D., Phyto, A.P., Tarning, J., et al. (2009) Artemisinin resistance in *Plasmodium falciparum* malaria. *New England Journal of Medicine*, 361(5): 455-467. DOI: [10.1056/NEJMoa0808859](https://doi.org/10.1056/NEJMoa0808859)
16. Ashley, E.A., Dhorda, M., Fairhurst, R.M., Amaratunga, C., Lim, P., Suon, S., et al. (2014) Spread of artemisinin resistance in *Plasmodium falciparum* malaria. *New England Journal of Medicine*, 371(5): 411-423. DOI: [10.1056/NEJMoa1314981](https://doi.org/10.1056/NEJMoa1314981)
17. Tun, K.M., Imwong, M., Lwin, K.M., Win, A.A., Hlaing, T.M., Hlaing, T., et al. (2015) Spread of artemisinin-resistant *Plasmodium falciparum* in Myanmar: a cross-sectional survey of the K13 molecular marker. *Lancet Infectious Diseases*, 15(4): 415-421. DOI: [10.1016/S1473-3099\(15\)70032-0](https://doi.org/10.1016/S1473-3099(15)70032-0)
18. van der Pluijm, R.W., Tripura, R., Hoglund, R.M., Pyae Phyto, A., Lek, D., ul Islam, A., et al. (2020) Triple artemisinin-based combination therapies versus artemisinin-based combination therapies for uncomplicated *Plasmodium falciparum* malaria: a multicentre, open-label, randomised clinical trial. *Lancet*, 395(10233): 1345-1360. DOI: [10.1016/S0140-6736\(20\)30552-3](https://doi.org/10.1016/S0140-6736(20)30552-3)
19. Scott, J.A., Berkley, J.A., Mwangi, I., Ochola, L., Uyoga, S., Macharia, A., et al. (2011) Relation between *falciparum* malaria and bacteraemia in Kenyan children: a population-based, case-control study and a longitudinal study. *Lancet*, 378(9799): 1316-1323. DOI: [10.1016/S0140-6736\(11\)60888-X](https://doi.org/10.1016/S0140-6736(11)60888-X)
20. Church, J., Maitland, K. (2014) Invasive bacterial co-infection in African children with *Plasmodium falciparum* malaria: a systematic review. *BMC Medicine*, 12: 31. DOI: [10.1186/1741-7015-12-31](https://doi.org/10.1186/1741-7015-12-31)
21. Bronzan, R.N., Taylor, T.E., Mwenechanya, J., Tembo, M., Kayira, K., Bwanaisa, L., et al. (2007) Bacteremia in Malawian children with severe malaria: prevalence, etiology, HIV coinfection, and outcome. *Journal of Infectious Diseases*, 195(6): 895-904.
22. Bassat, Q., Guinovart, C., Sigauque, B., Aide, P., Sacarlal, J., Nhampossa, T., et al. (2009) Severe malaria and concomitant bacteraemia in children admitted to a rural Mozambican hospital. *Tropical Medicine & International Health*, 14(9): 1011-1019. DOI: [10.1111/j.1365-3156.2009.02326.x](https://doi.org/10.1111/j.1365-3156.2009.02326.x)
23. Were, T., Davenport, G.C., Yamo, E.O., Hittner, J.B., Awandare, G.A., Otieno, M.F., et al. (2011) Bacteremia in Kenyan children presenting with malaria. *Journal of Clinical Microbiology*, 49(2): 671-676. DOI: [10.1128/JCM.01864-10](https://doi.org/10.1128/JCM.01864-10)
24. Maitland, K., Kiguli, S., Opoka, R.O., Engoru, C., Olupot-Olupot, P., Akech, S.O., et al. (2011) Mortality after fluid bolus in African children with severe infection. *New England Journal of Medicine*, 364(26): 2483-2495. DOI: [10.1056/NEJMoa1101549](https://doi.org/10.1056/NEJMoa1101549)
25. Chico, R.M., Pittrof, R., Greenwood, B., Chandramohan, D. (2008) Azithromycin-chloroquine and the intermittent preventive treatment of malaria in pregnancy. *Malaria Journal*, 7: 255. DOI: [10.1186/1475-2875-7-255](https://doi.org/10.1186/1475-2875-7-255)
26. Kimani, J., Phiri, K., Kamiza, S., Duparc, S., Ayoub, A., Rojo, R., et al. (2016) Efficacy and safety of azithromycin-chloroquine versus sulfadoxine-pyrimethamine for intermittent preventive treatment of *Plasmodium falciparum* malaria infection in pregnant women in Africa: an open-label, randomized trial. *PLOS ONE*, 11(6): e0157045. DOI: [10.1371/journal.pone.0157045](https://doi.org/10.1371/journal.pone.0157045)