INTERDISPLINARY NOTE

Interventions against *Plasmodium falciparum* carriage in the Sahel: Evidence to improve seasonal malaria control

Betty Kazanga

Supervisor: Prof Jean Gaudart

Co- supervisor: Dr Jordi Landier

Doctoral School 659- Biomedical Research, Aix-Marseille Université

UMR 1252 SESSTIM (Sciences Economiques et Sociales de la Santé & Traitement de l'Information Médicale)

This thesis was prepared in the framework of the Doctoral Network of Public Health coordinated by the École des Hautes Études en Santé Publique (EHESP).

Abstract

Malaria transmission in the Sahel has declined substantially over the past two decades following the scale-up of vector control, improved access to diagnosis and treatment, and seasonal malaria chemoprevention (SMC). Despite these gains, transmission persists in many settings. This persistence increasingly reflects not failure of interventions, but a evolving malaria epidemiology under sustained control pressure, characterised by the growing importance of asymptomatic and low-density *Plasmodium falciparum* infections.

This thesis aimed to understand how malaria persists in highly seasonal Sahelian settings despite large-scale intervention deployment, and to identify opportunities for improving and adapting control strategies. Using routine surveillance data from Senegal and longitudinal cohort data from the Malaria Asymptomatic Reservoirs in the Sahel (MARS) project in Mali and Senegal. The work examined (i) the temporal alignment between SMC delivery and malaria incidence, (ii) the age distribution and seasonal dynamics of parasite carriage, and (iii) the determinants of persistent infection.

The findings show that while SMC effectively reduces clinical malaria in targeted populations, its impact is constrained by imperfect alignment with local transmission dynamics, resulting in periods of vulnerability. At the same time, malaria epidemiology progressively evolving, with parasite carriage increasingly concentrated in older children and adolescents and dominated by asymptomatic and frequently subpatent infections. These infections persist across seasons and are likely to sustain transmission despite reductions in clinical burden.

By integrating epidemiological, environmental, and operational perspectives, this work highlights the need to move beyond uniform intervention strategies toward more adaptive and context-specific approaches. These include optimizing SMC timing and duration and developing complementary strategies targeting the asymptomatic parasite reservoir. Overall, this thesis contributes to a reframing of malaria control in the Sahel as a dynamic process requiring continuous adaptation to evolving transmission systems.

Introduction

Over the past two decades, malaria control efforts in sub-Saharan Africa have led to substantial reductions in morbidity and mortality [1,2]. In the Sahel, where transmission is highly seasonal and concentrated within a limited period each year [3], this progress has been driven by the combined scale-up of vector control interventions, improved access to diagnosis and treatment, and the deployment of seasonal malaria chemoprevention (SMC) [2,4]. SMC consists of the monthly administration of antimalarial drugs to young children under 5 years of age, and up to 10 years in some settings, during the rainy season, regardless of infection status, to prevent clinical malaria [4,5]. Together, these strategies have significantly reduced the burden of clinical malaria, particularly among young children [1,6].

Despite these advances, malaria transmission persists across many Sahelian settings . In several high-burden regions, progress has slowed or plateaued in recent years [1,2], raising important questions about the limits of current control strategies. While persistent transmission has often been attributed to incomplete coverage, operational constraints, or emerging biological threats such as insecticide and drug resistance [7], there is growing recognition that these explanations are only partial. Increasingly, malaria persistence appears to be linked to changes in the underlying epidemiology of infection under sustained intervention pressure [8,9].

In highly seasonal transmission systems, the relationship between infection, disease, and immunity is complex. Repeated exposure over successive transmission seasons leads to the gradual acquisition of partial immunity, which reduces the risk of clinical disease without preventing infection [10]. As a result, a substantial proportion of *Plasmodium falciparum* infections remain asymptomatic, often at low density and frequently undetected by routine diagnostic tools[8]. These infections can persist over time, including across dry seasons, and constitute a reservoir that may contribute to ongoing transmission despite reductions in clinical incidence [11,12].

The scale-up of SMC has further altered the epidemiological context. By providing chemoprophylaxis to young children during the peak transmission period, SMC has become a central component of malaria prevention in the Sahel [4] However, its impact depends on how the intervention interacts with other determinants of infection, including age, seasonality, and patterns of exposure. At the same time, malaria transmission in the Sahel remains characterised by marked spatial heterogeneity and population mobility[13], which can complicate the interpretation of surveillance data and the design of interventions.

Taken together, these elements highlight the need to better understand how malaria transmission is maintained in highly seasonal settings under sustained intervention pressure. This requires moving beyond a focus on clinical cases alone to consider the broader structure and dynamics of infection, including asymptomatic carriage and its determinants.

Main findings

This work provides an integrated analysis of malaria persistence in highly seasonal Sahelian settings, focusing on the interaction between SMC intervention deployment, infection dynamics, and population characteristics. Three main dimensions emerge from the findings.

First, the effectiveness of SMC is closely linked to its temporal alignment with local transmission dynamics. Analyses of routine surveillance data in southeastern Senegal, where SMC is delivered to children under 10 years of age, indicate that under real-world programme conditions, protection is highest during the first three weeks following each round and declines thereafter. When the timing and spacing of rounds are not fully aligned with the duration and dynamics of the transmission season, protection becomes uneven over time, resulting in periods during which targeted children are less protected.

Second, the distribution of *Plasmodium falciparum* infection appears structured by age and characterised by a high prevalence of asymptomatic carriage. In the Malian study sites, where SMC targets children under 5 years of age, parasite carriage was observed across a broad age range, with higher prevalence among older children and young adults not targeted by the intervention. Most infections were asymptomatic and of low density, and were detected in both rainy and dry seasons, suggesting ongoing parasite circulation beyond peak transmission periods.

Third, exploratory analyses suggest that patterns of human mobility may contribute to the distribution of infection across space. Although these analyses remain preliminary, they indicate that recent travel may be associated with parasite carriage, supporting the hypothesis that population movement may play a role in connecting areas with different transmission intensities.

Interdisciplinary perspectives

Understanding malaria persistence in the Sahel requires moving beyond a single disciplinary perspective. The findings of this thesis highlight how the interaction between intervention design and implementation, infection dynamics, and population behaviour reshapes transmission patterns, and call for an integrated approach combining epidemiology, data science, social sciences, health policy, and health economics.

From an epidemiological perspective, the results illustrate how sustained intervention pressure can modify the distribution of infection within populations. While reductions in clinical malaria among young children reflect the success of SMC [5,6], the persistence of asymptomatic and low-density infections across a broader age range suggests that transmission is increasingly maintained outside the population targeted by SMC [14,15]. This highlights the need to consider infection dynamics beyond clinical case patterns and to better characterise the structure of the parasite reservoir.

From a data science and analytical perspective, this work underscores the value of high-resolution temporal and longitudinal data for understanding malaria dynamics in seasonal settings. The identification of variations in protection following SMC rounds illustrates how routine surveillance data can be used to assess intervention performance under real-world conditions. Similarly, cohort-based analyses provide insights into infection patterns that are not captured through routine diagnostics [14]. Together, these approaches highlight the importance of integrating multiple data sources to better capture the complexity of malaria transmission.

From a social and behavioural sciences perspective, the findings point to the role of human behaviour and mobility in shaping exposure to infection. Patterns of movement, care-seeking behaviour, and adherence to interventions influence both individual risk and the broader distribution of infection within populations. In contexts characterised by spatial heterogeneity in transmission, these factors may contribute to disconnects between place of residence and place of exposure, complicating both surveillance and intervention design [13].

From a health policy and implementation perspective, the results emphasise the importance of aligning intervention strategies with local epidemiological and operational realities. The temporal patterns observed in relation to SMC delivery highlight the sensitivity of intervention effectiveness to timing, spacing, and coverage. At the same time, the persistence of infection outside targeted groups raises questions about the scope and targeting of existing strategies. These findings point to

the need for more flexible and context-specific approaches that can adapt to local transmission dynamics and evolving epidemiological patterns.

From a health economics perspective, these findings highlight the importance of considering malaria control within the broader context of health system financing, resource allocation, and competing priorities. Interventions such as SMC, which target young children at highest risk of severe disease, can reduce both morbidity and associated healthcare costs. However, they are implemented as part of a wider package of interventions, including vector control, case management, and surveillance [1], and should be assessed within this broader context. Changes in the distribution of infection across age groups also observed in other studies in the Sahel [14,15] further raise questions about how well the allocation of resources across malaria interventions aligns with evolving patterns of risk and transmission. Decisions regarding intervention design, timing, and targeting therefore need to be considered in relation to overall programme objectives and available health budgets, taking into account interactions between different components of the control strategy.

Taken together, these perspectives suggest that malaria persistence in the Sahel arises from interactions between intervention design, infection dynamics, and population behaviours across temporal and spatial scales. This complexity challenges approaches that rely on fixed assumptions about risk, target populations, or transmission patterns, and highlights the need for strategies that can respond to changing epidemiological contexts.

Public health challenges and implications

The findings of this work point to several important considerations for malaria control in highly seasonal Sahelian settings, which arise not from the absence of effective interventions, but from the increasing complexity of transmission dynamics under sustained control.

Firstly, it is important to consider how intervention strategies can be adapted to variable transmission patterns. In practice, malaria control programmes rely on standardised delivery schedules, yet transmission intensity and duration vary across locations and over time [3,16]. This makes it difficult to balance operational feasibility with epidemiological responsiveness, and limits the extent to which flexibility can be introduced into intervention design without compromising programme delivery.

Secondly, the age-structured distribution of clinical burden and parasite carriage under SMC intervention pressure suggests that strategies targeting the reservoir, such as mass drug administration (MDA), could complement existing interventions to reduce transmission [17,18]. However, the implementation of such approaches presents several challenges, including their cost and sustainability, potential implications for drug resistance, operational complexity, and issues related to acceptability and adherence within communities [18–20]. These considerations highlight the need for careful evaluation of how reservoir-targeting strategies could be integrated into existing control programmes.

Lastly, as transmission becomes more heterogeneous and shaped by population movement, approaches based on fixed geographic targeting may become less well suited to capturing patterns of exposure[13]. This raises operational questions regarding how surveillance systems and intervention strategies can account for mobility and spatial variability in a feasible and scalable way.

More broadly, these challenges reflect the complexity of designing malaria control strategies in settings where transmission is not uniformly distributed across time, space, or population groups. They point to the limits of approaches based on uniform assumptions and highlight the need for decision-making frameworks that can accommodate changing epidemiological conditions while remaining operationally viable.

Conclusion

Malaria control in the Sahel has substantially reduced clinical burden, particularly among young children. However, these findings suggest that persistent transmission reflects a transformation of malaria epidemiology under sustained intervention pressure rather than a failure of current strategies. Changes in the temporal, spatial, and population distribution of infection highlight the need for more adaptive approaches to malaria control.

Future strategies will need to better align intervention timing, target the broader infection reservoir, and account for spatial heterogeneity and population movement. Sustaining progress will depend on the ability to adapt control strategies to increasingly complex and evolving transmission dynamics.

References

1. World Health Organization. World malaria report 2025: Addressing the threat of antimalarial drug resistance [Internet]. Geneva: World Health Organization; 2025. Available from: https://www.who.int/publications/i/item/9789240117822

2. Bhatt S, Weiss DJ, Cameron E, Bisanzio D, Mappin B, Dalrymple U, et al. The effect of malaria control on Plasmodium falciparum in Africa between 2000 and 2015. Nature. 2015 Oct;526(7572):207–11. doi:10.1038/nature15535

3. Yamba EI, Fink AH, Badu K, Asare EO, Tompkins AM, Amekudzi LK. Climate Drivers of Malaria Transmission Seasonality and Their Relative Importance in Sub-Saharan Africa. GeoHealth. 2023 Feb;7(2):e2022GH000698. doi:10.1029/2022GH000698

4. World Health Organization. WHO policy recommendation: seasonal malaria chemoprevention (SMC) for plasmodium falciparum malaria control in highly seasonal transmission areas of the Sahel sub-region in Africa [Internet]. Geneva: World Health Organization; 2012. Located at: WHO IRIS. Available from: https://apps.who.int/iris/handle/10665/337978

5. Cissé B, Ba EH, Sokhna C, NDiaye JL, Gomis JF, Dial Y, et al. Effectiveness of Seasonal Malaria Chemoprevention in Children under Ten Years of Age in Senegal: A Stepped-Wedge Cluster-Randomised Trial. Noor AM, editor. PLoS Med. 2016 Nov 22;13(11):e1002175. doi:10.1371/journal.pmed.1002175

6. Baba E, Hamade P, Kivumbi H, Marasciulo M, Maxwell K, Moroso D, et al. Effectiveness of seasonal malaria chemoprevention at scale in west and central Africa: an observational study. The Lancet. 2020 Dec;396(10265):1829–40. doi:10.1016/S0140-6736(20)32227-3

7. Oxborough RM, Chilito KLF, Tokponnon F, Messenger LA. Malaria vector control in sub-Saharan Africa: complex trade-offs to combat the growing threat of insecticide resistance. The Lancet Planetary Health. 2024 Oct;8(10):e804–12. doi:10.1016/S2542-5196(24)00172-4

8. Bousema T, Okell L, Felger I, Drakeley C. Asymptomatic malaria infections: detectability, transmissibility and public health relevance. Nat Rev Microbiol. 2014 Dec;12(12):833–40. doi:10.1038/nrmicro3364

9. Andolina C, Rek JC, Briggs J, Okoth J, Musiime A, Ramjith J, et al. Sources of persistent malaria transmission in a setting with effective malaria control in eastern Uganda: a longitudinal, observational cohort study. Lancet Infect Dis. 2021 Nov;21(11):1568–78. doi:10.1016/S1473-3099(21)00072-4 PubMed PMID: 34146476; PubMed Central PMCID: PMC8554388.

10. Rodriguez-Barraquer I, Arinaitwe E, Jagannathan P, Kamya MR, Rosenthal PJ, Rek J, et al. Quantification of anti-parasite and anti-disease immunity to malaria as a function of age and exposure. eLife. 2018 Jul 25;7:e35832. doi:10.7554/eLife.35832

11. Lindblade KA, Steinhardt L, Samuels A, Kachur SP, Slutsker L. The silent threat: asymptomatic parasitemia and malaria transmission. Expert Rev Anti Infect Ther. 2013 Jun;11(6):623–39. doi:10.1586/eri.13.45 PubMed PMID: 23750733.

12. Coulibaly D, Travassos MA, Tolo Y, Laurens MB, Kone AK, Traore K, et al. Spatio-Temporal Dynamics of Asymptomatic Malaria: Bridging the Gap Between Annual Malaria Resurgences in a Sahelian Environment. The American Journal of Tropical Medicine and Hygiene. 2017 Dec 6;97(6):1761–9. doi:10.4269/ajtmh.17-0074

13. Wesolowski A, Eagle N, Tatem AJ, Smith DL, Noor AM, Snow RW, et al. Quantifying the Impact of Human Mobility on Malaria. Science. 2012 Oct 12;338(6104):267–70. doi:10.1126/science.1223467

14. Legendre E, Ciré Ba EHK, L'Ollivier C, Cissoko M, Katile A, Mehadji M, et al. Plasmodium falciparum carriage in a population under long-term, intensive malaria control in Kedougou region, Senegal: a 1-year cohort study. The Lancet Global Health. 2025 Nov;13(11):e1935–45. doi:10.1016/S2214-109X(25)00271-2

15. Manga IA, Mhadji A, Lam A, Diouf MP, Minlekib PC, Tairou F, et al. Asymptomatic carriage of Plasmodium falciparum in children no longer targeted for seasonal malaria chemoprevention and with a history of exposure to this strategy: A cross sectional study in southern Senegal. Vieira JLF, editor. PLoS ONE. 2025 Mar 25;20(3):e0318037. doi:10.1371/journal.pone.0318037

16. Diouf I, Rodriguez Fonseca B, Caminade C, Thiaw WM, Deme A, Morse AP, et al. Climate Variability and Malaria over West Africa. Am J Trop Med Hyg. 2020 May;102(5):1037–47. doi:10.4269/ajtmh.19-0062 PubMed PMID: 32189612; PubMed Central PMCID: PMC7204584.

17. Ba E hadji, Roh ME, Diallo A, Gadiaga T, Seck A, Thiam S, et al. Effect of mass drug administration on malaria incidence in southeast Senegal during 2020–22: a two-arm, open-label, cluster-randomised controlled trial. The Lancet Infectious Diseases. 2025 Jun;25(6):656–67. doi:10.1016/S1473-3099(24)00741-2

18. Schneider ZD, Shah MP, Boily MC, Busbee AL, Hwang J, Lindblade KA, et al. Mass Drug Administration to Reduce Malaria Transmission: A Systematic Review and Meta-Analysis. Am J Trop Med Hyg. 2024 Apr;110(4 Suppl):17–29. doi:10.4269/ajtmh.22-0766 PubMed PMID: 38118174; PubMed Central PMCID: PMC10993786.

19. Legendre E, Ndiaye A, Sougou NM, Gaudart J, Ba EH, Ridde V, et al. Prospective acceptability of mass drug administration for malaria in Kedougou region in Senegal: a mixed method study. Malar J. 2024 Sep 16;23(1):279. doi:10.1186/s12936-024-05078-8

20. Amimo F, Lambert B, Magit A, Sacarlal J, Hashizume M, Shibuya K. *Plasmodium falciparum* resistance to sulfadoxine-pyrimethamine in Africa: a systematic analysis of national trends. BMJ Glob Health. 2020 Nov;5(11):e003217. doi:10.1136/bmjgh-2020-003217