**Title:** Emerging properties of malaria transmission and persistence in urban Accra, Ghana: Evidence from a participatory system approach

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Abstract

Several studies that aim to enhance the understanding of malaria transmission and persistence in urban settings failed to address its underlining complexity. We aim at doing that by applying a qualitative and participatory-based system analysis and mapping to elicit the system’s emergent properties. In two experts’ workshops, we sketched and refined the system, which was represented through a causal loop diagram, where the identification of leverage points was done using network analysis. We found 45 determinants interplaying through 56 linkages, and identified three subsystems: urbanization-related transmission, infection-prone behavior and healthcare efficiency, and Plasmodium resistance. Apart from the number of breeding sites and malaria positive cases, other determinants such as drug prescription and the awareness of householders were identified by the network analysis as leverage points and emergent properties of the system of transmission and persistence of malaria. Based on our findings, we suggest that ongoing efforts to control malaria, such as the use of insecticide-treated bed nets and larvicide applications should continue, and include new ones focusing on the public awareness and malaria literacy of city dwellers. We found that our participatory approach strengthened the legitimacy of the recommendations and the co-learning of participants.

Keywords: Network analysis, causal loop diagram, emergence, urban, complex system.
Background

Malaria is still the number one deadliest infectious disease, responsible for more than 380,000 deaths in 2018 only [1]. In endemic areas of sub-Saharan Africa (SSA), the expenses for its control and prevention reach up to 40% of all public health expenditures [2], and its effects were estimated to have reduced the GDP by 9% in 2010 in affected countries in SSA [3]. Due to the collaborative efforts of governments and development partners, malaria mortality has been reduced by 66% from 2007 to 2017 [4], but the challenge is yet far from being solved.

Africa’s population is expected to triple by 2050 [5], with major growth occurring in urban areas. For example, the population of major Ghanaian cities has grown by 3.5% per annum from 1984 to 2010 [6]. As urbanization brings along challenges, such as traffic congestion, slumming, and pollution, little priority is given to public health-related issues [7]. For example, in Accra, the capital of Ghana, city planning issues often overshadow the health-related ones, with the local government investing less than 50USD per person per year on health [8]. Moreover, the poorest communities experience the greatest harm [8], like Accra’s head porters, especially challenged by the nature of their work and often not able to afford the national insurance scheme [9].

A pressing public health issue is the prevalence of vector-borne diseases, like malaria [10,11]. Its predominant vector *Anopheles gambiae*, whose customary habitat for reproduction used to be rural, clean, and shallow water ponds surrounded by grassy fields, has now adapted to the urban conditions and prospers in polluted waters, such as clogged gutters or puddles, characteristic of poor urban housing [10,12].

This example evidences the complex and adaptive character of the malaria transmission system, where the humans, vectors, the environment, and parasites interact in an iterative and nonlinear manner [13]. Earlier modeling approaches rarely considered such complexity, and instead conceived transmission causal and unilaterally, which contributed to the development of policies
favoring the promotion of single-intervention programs, like the free provision of malaria drugs [14–16].

A complex system is one where its components, apparently disconnected and performing their roles after their interests, align together to perform more sophisticated functions [17]. This tends to be the case for most social and ecological phenomena, as they do not occur in isolation but intermingled [18]. The unraveling of complex systems is operationalized through approaches, methods, and tools that instead of assessing the determinants individually, focus on the interactions among them, and the overall function of the system [19]. In that regard, the involvement of local stakeholders appears key, as it reduces the bias of researchers and increases the legitimacy of the outcomes [20].

We have applied such approaches in this study and visualized the interactions among the determinants of malaria transmission in urban conditions using a Causal Loop Diagram (CLD) and displayed emergent properties of the system via Network Analysis (NA).

CLD can support the visualization of the interplay among determinants and assist in the identification of causal relationships among them [21]. Moreover, to better understand the complexity in malaria transmission, CLD can also help to devise improved strategies for more effective control of the disease in cities (and beyond) by scouting underplayed channels [13].

NA is based on the principles of network theory, where a system is considered a web of edges (interactions) that connect the nodes (determinants) [22]. The examination of the network properties (e.g. density) and its topology, e.g. centrality, indicate the nature of the information flow and reveal the most sensitive determinants and their roles [23,24]. Furthermore, by applying graph theory, NA offers powerful visualizations of the analyzed phenomena [22,25]. A successful application of NA can display some emerging properties of complex systems, such as
McGlashan [24] did in identifying the leverage points, i.e., where one can intervene to alter the system of childhood obesity in Australia.

We hypothesized that by combining participatory CLD and NA we would be able to better accomplish the aims of this study, that are (i) to understand the interplay between determinants of the system of transmission and persistence of malaria in urban settings, and subsequently (ii) to identify its emerging properties (i.e., properties of the network and leverage points of the system and derive potential interventions on the system).

**Methods**

**Study area**

Accra, the capital city of Ghana, is located on the coast of the West African Golf of Guinea. Its climate is tropical alternating wet and dry phases, mainly due to the cyclical harmattan winds. The average annual rainfall is 730mm and bimodally distributed, the temperature average reaches 26.6°C, and the relative humidity rounds 81%, with little variations along the year [26,27]. Accra’s current population is 2.3 million, to a great extent composed of migrants from successive waves of rural-urban migration across the last 50 years. Housing is uneven in infrastructure quality and service provision, but standards are generally low. The worst affected areas are old central neighborhoods, where slums abound, and peripheral settlements, where new developments happen [28].

Although malaria is traditionally considered a predominantly country-side disease, recent evidence showed that mortality and morbidity in SSA’s cities are high [26]. For example, in Accra, slums and poorly-managed urban areas such as James-Town and Korle-Dudor districts recorded the highest malaria indices of morbidity and mortality [29].
Identification of key experts and Causal Loop Diagram elicitation

Initially, we held an informal meeting with district assembly members of James-Town and Korle-Dudor districts and other members of the communities, to identify the key institutions and experts working on the prevention and treatment of malaria. The list of institutions and experts was consolidated to include twelve representatives from the Ghana National Malaria Program, Malaria Initiative/USAID, World Health Organization, Ghana Health Service, Plant Protection and Regulatory Services/Ministry of Food and Agriculture, Noguchi Memorial Institute for Medical Research, several NGOs, and local healthcare facilities.

The experts met in two recorded workshops, which were facilitated by a modeling team (modeler, facilitator, and wall-builder) following Hovmand’s guidelines [30]. In the first workshop, we refined the problem, defined the variables of the model, and drew an initial CLD. A CLD aims to show the interplay between components of a complex system, eliciting the feedback loops, and facilitate the understanding of a given problem [31,32]. For that, we set the background by presenting the outcomes of precedent informal interviews; then, together with the experts, the boundaries of the malaria-related transmission and persistence CLD were defined.

Secondly, experts and the modeling team identified a list of determinants explaining the transmission and persistence of malaria and elicited a cause-effect map from the interactions between determinants. A cause in the CLD represents a determinant from which the arrow emerges, and the effect is a determinant that receives the arrow. The positive or negative sign of the arrow explains the type of association, i.e., a cause A implying an effect B showing a positive sign should be read: The increase in A implies an increase in B. Inversely, A implying B with a negative sign should be read: An increase in A causes a decrease in B (Fig. 1). Subsequently,
determinants that were not relevant were excluded, e.g., indoor residual spray, which is not used in Accra.

During the second workshop, together with experts, we proceeded to the validation and refinement of the CLD. In consequence, new determinants were added whereas others were merged into more inclusive ones, and some determinants judged non-relevant were removed, which led to changes in the causal linkages. The model obtained (Suppl. Fig. 1) was further refined by the modeling team, which focused on the identification of feedback loops in the CLD (Suppl. Table 1).

**Network analysis**

The emerging properties of the system represented by the CLD were displayed by the properties of the network and its most central determinants. The most central determinants stand for the leverage points for transmission and persistence of malaria in Accra. These points can enhance the control of malaria when they are adjusted according to the properties displayed by the system.

The CLD represents an unweighted directed network, where the connectivity is represented by the adjacency non-symmetric and unweighted matrix $A_{ij}$ (Eq. 1) [24]

$$A_{ij} = \begin{cases} 1 & \text{if i causally influences j} \\ 0 & \text{otherwise} \end{cases}$$  \hspace{1cm} (1)

The properties of the network were estimated through the computation of the density, the average path length, and the modularity of the CLD network. The functional importance of the determinants was captured via the calculation of six measures of centrality, i.e., degree ($K$), in-degree ($K^{in}$), out-degree ($K^{out}$), PageRank ($x$), closeness ($C$), and betweenness ($B$).

The degree centrality ($K$) assesses the determinants' connectivity. With respect to the adjacency matrix, the degree $k_i$ can be calculated for a network containing $n$ nodes:
Since the causal diagram is assimilated to a directed network, Eq. 2 can be re-written as

\[ k_i^{in} = \sum_{j=1}^{n} A_{ij}, \quad k_i^{out} = \sum_{i=1}^{n} A_{ij}, \]  

where \( k_i^{in} \) and \( k_i^{out} \) stand for in-degree and out-degree centrality if there is connectivity from \( j \) to \( i \), which indicates the direction of the connection between determinants, the former as a recipient (effect), and the latter as emitter (cause).

PageRank eigenvector centrality \( x_i \) value estimates the influence of certain determinants on the whole network [33,34] and is given by

\[ x_i = 0.85 \times \sum_{l} A_{ij} \frac{b_i}{k_i^{out}} \]

where \( x_i \) is the out-degree of the node \( i \). Thus, \( b_l \) is given by \( b_l = \{0 \text{ if in-degree otherwise } 1\} \).

The closeness centrality \( C_i \) calculates the proximity among determinants and identifies which is the one closest to all others in the network [23,34–36]. \( C_i \) is defined by

\[ C_i = \sum_{ij} \frac{n}{g_{ij}} \]

where \( n \) represents the total number of the shortest paths (the shortest self-avoiding route that runs from one determinant to another along with the connectivity [34]) between the determinant \( i \) and \( j \), and \( g_{ij} \) is each elementary shortest path or the distance between the determinants \( i \) and \( j \).

The betweenness centrality \( B_i \) measures how a determinant is favorably located to connect other determinants of the network [24,33,34,37]. Assuming that \( g_{st} \) is the total number of shortest paths from \( s \) to \( t \) then \( n_{st}^i \) is the number of shortest paths from the determinants \( s \) to \( t \). Simply
\[ n_{st}^i = \begin{cases} 1 & \text{if there is a relationship between } s \text{ and } t \\ 0 & \text{otherwise} \end{cases} \]

The computation of \( B_i \) is given by

\[ B_i = \sum_{st} \frac{n_{st}^i}{g_{st}} \] (6)

All the analyses were run using R [38].

All participants involved in this study were informed and signed their consent for the recording and the use of the meetings’ materials for scientific purposes.

**Results**

*A system model of malaria transmission and persistence*

The transmission and persistence of malaria in Accra are portrayed in a CLD of the complex system model, entailing 56 interactions among 45 determinants. This model shows three sub-models triggered each by a reinforcing loop, i.e., (i) the urbanization-related transmission and acquired resistance of *Anopheles* to insecticides (green), (ii) the human’s infection-prone behavior (red), and (iii) the healthcare efficiency and *Plasmodium* resistance (blue) (Fig1).

*Urbanization-related transmission and resistance of Anopheles to insecticides*

The deficient city planning and the planning enforcement, inadequate housing conditions, and limited waste and sewage infrastructure lead to the proliferation of *Anopheles* breeding sites, which is worsened by the excavation of wells for urban and peri-urban agriculture and rainfall. Besides, a temperature range between 26 and 33°C in Accra, contributes to the increase in the reproductive rate of *Anopheles*, their absolute numbers, and finally their survival, augmenting the risk of infection.

Furthermore, the preventive use of insecticides in households, agricultural sites, and hospitals leaves residues all contribute to the development of insecticide resistance in local mosquito populations. Thus, in the reinforcing loop one (R1, Fig1), we observe that the transmission of
malaria depends not only on the environmental factors, such as temperature and rainfall but also on the lack of regulations to prevent and control the proliferation of mosquito breeding sites. These effects are exacerbated by the widespread use of insecticides. Hence, this reinforcing loop portrayed the environment as a pathway of both, the infection and the development of resistance of mosquitoes to insecticides (Fig. 1).

*Humans infection-prone behavior*

At the individual and household levels, ideally, the awareness of malaria risk leads to the reduction of nighttime activities, as well as the use of protective/preventive measures against mosquito bites, such as the use of insect-proof mesh for doors and windows and insecticide-treated bed-nets (ITNs). The more these measures are accepted and used, the lower the infection will be. In addition, human migration increases the number of infected cases by importation. More infected people in Accra imply a greater number of mosquitoes becoming infected that will subsequently transmit the pathogens to new hosts. This reinforcing loop two (R2, Fig 1) highlights the importance of individual and household decisions, and how a changing behavior can prevent the transmission and its persistence by, for instance, reducing the nighttime activities and using protective measures like ITNs. (Fig 1.).

*Healthcare efficiency and Plasmodium resistance*

Malaria carriers can be asymptomatic, and as Ghana’s healthcare system is often unable to detect them, they frequently remain untreated and thus keep spreading the disease. Knowledge of malaria symptomatology and a sufficient household income lead to more visits to healthcare facilities. If healthcare workers are well trained, adhere to prescription protocols, and patients comply with the prescribed treatment, the reinforcing loop three (R3, Fig 1) will operate, and trust in the health system will grow. If not, the use of inadequate medication will increase,
alongside the resistance of the *Plasmodium* parasite to preventive and curative drugs. Besides, the free availability of heavily subsidized drug treatments augments self-medication and indirectly enhances drug-resistance development in *Plasmodium*. This loop reveals that a good healthcare system requires to be well endowed logistically and in terms of personnel. Substituting such a healthcare system with highly accessible low-priced drugs can increase the prevalence of resistant strains of *Plasmodium*. Moreover, this loop revealed an unintended pathway of malaria treatment policies [30], which, although well-intentioned, can be counter-productive. Relatedly, symptomatic patients, unsatisfied with allopathic treatments and drug resistance, may opt for alternative medicines, despite its often uncertain outcomes.

[Insert Fig 1 here]

**Fig. 1:** Causal loop diagram depicting the complexity in malaria transmission and persistence in Accra (Ghana). In green the urbanization-related transmission sub-model, in red the human's infection-prone behavior of malaria sub-model, and the healthcare efficiency and *Plasmodium* resistance sub-model (blue)

**Network analysis of the CLD**

**Properties of the network**

The network representing the CLD displayed a structure of *small-world*, meaning that all determinants are not interconnected but are anyhow reachable by a small number of steps [39]. It shows an average path of 6.309, meaning that each determinant can reach any other in average through 6.309 paths. Still, it has a low density (0.028), presenting only 2.8% of possible edges in a completely interconnected network, and suggesting that a change in a determinant will have only a limited impact on the whole system. This indicates that despite its apparent complexity,
there is a small connection path among determinants, allowing the information to spread rapidly [24,40]. Furthermore, a modularity of 0.619 implies a structural clustering among determinants, indicating that acting on the determinants of the highest betweenness will have a spillover effect on the whole system [24]. In other words, an effective way to impulse a change in the system is to induce a change in the mediator.

*Network metrics*

The CLD has a *scale-free* distribution, meaning that its in-degree and out-degree metrics showed a heavy-tailed distribution with values ranging from 0 to 5 (Suppl. Fig. 2). Few nodes show 0 out-degree, indicating that most of the determinants influence other determinants. This configuration describes well real-world networks and suggests a high resilience of the system [41] (Table 1 & Suppl. Fig. 2). Thus, beyond the mediator of the system, the other leverage points also needed to be strategically adjusted to efficiently finetune the system.

The network centrality metrics revealed that *malaria positive cases*, was the determinant of higher centrality, either impacting or been impacted by seven determinants. Also, the *number of breeding sites* was impacted by five other determinants, \(k^\text{in} = 5\) namely: 1. *more rainfall*, 2. the *hygiene and sanitation of householders’ compound*, 3. the *adequate housing construction*, 4. a *convenient waste and sewage management*, and 5. the *wells excavation*. Conversely, the *householders’ awareness and decision-making on malaria infection risk* was the main cause of transmission and persistence, as it impacts five other determinants \(k^\text{out} = 5\) namely 1. the *hygiene and sanitation of household compound*, 2. the *use of ITN*, 3. the *frequency and duration of nighttime activities*, 4. the *use of door and windows mesh*, and 5. *self-medication*.

Predictably, the determinant of highest betweenness that connects most clusters of determinants is the *malaria positive cases* \(B = 328\); and the one with the highest Page rank, and, thus, the
most influential is the *malaria positive cases* \( (x = 0.086) \). Also, the determinant with the greatest closeness centrality, i.e., with the shortest distance to all others is *drug prescription* \( (C = 0.381) \) (Table 1).

Interestingly, determinants participating directly in the infection process, such as the *number of breeding sites*, the *malaria positive cases*, or not, such as the *drug prescription* and *householders' awareness and decision-making on malaria infection risk* are also important leverage points (influential points in the system where a small change in these determinants can induce a big change in the whole system [42]) that can affect the system.

[Insert Table 1 here]

**Discussion**

*System model of malaria transmission and persistence in Accra*

We found that the most central determinants also standing for the leverage points of the system, aside from the environmental-related ones, are those resulting from the citizens’ *awareness of malaria infection risks*, and *household income*, and derived empowerment. These findings corroborate earlier studies that showed that poor-income households are more vulnerable to the disease, by facing a double burden: Malaria hotspots in Accra are in economically deprived communities, where malaria infection risk is additionally fueled by the economic needs, leading to community members to take up jobs that increase their exposure [43]; and, poor-income households spend relatively more of their earnings on the treatment of malaria than the higher-income ones [44].

Our results also stress the importance of an efficient healthcare system, a structural issue in most countries of the Global South. We found particularly relevant the *trust in the healthcare system*, which can be reinforced through *training and supervision of health workers* on malaria diagnosis.
and treatment-related protocols, and the adherence of the health workers to it. Supporting this, a system dynamics simulation on policies for improving neonatal health in Uganda demonstrated that the workload of healthcare workers affects the development of trust of patients, especially when it leads to long waiting times for attention [45]. Likewise, a study in England and Wales revealed that the reduction of waiting-time built the trust of patients and enhanced healthcare efficiency [46]. On the other hand, the non-adherence to the prescription and treatment protocols by health workers can lead communities to underestimate malaria infection and increase its effects, which augments the distrust in the health system.

Relatedly, we found that the subsidy on anti-malaria drugs instead of promoting a more holistic public health policy contributes to patients’ self-medication [47], highlighting the sometimes counterproductive effects of a sole focus of public health programs on biomedical policies as this ignores the complexity of malaria transmission [48]. Previous research showed that patients’ self-medication leads to arbitrary dosage and posology of anti-malaria drugs, and tends to exacerbate the symptoms and augments the morbidity and mortality of malaria [49]. Such situations are worse in poor-income households, where people often self-medicate with inadequate or counterfeit drugs, and/or inappropriate dosages and posologies at the onset of malaria symptoms [47].

Humans can be infected with *P. falciparum* and be symptomatic or asymptomatic. The latter is most often undiagnosed, among others, because its testing is costly [50]. That is the reason why many public health systems tend to neglect them, thereby contributing to the persistence of malaria [51]. Also, imported cases by human migration amplify the number of cases in cities and at times can initiate the resurgence of malaria in locations where it had been previously under control [52,53].
Our findings also suggest that deficient urban sanitation and poor urban planning increase the number of mosquito breeding sites. About 10% of Anopheles mosquitoes breeding sites in Accra are situated around construction sites [12]. Similar observations were made in Nigeria and Tanzania, where clogged gutters and sewage channels are playing similar roles [55]. Thus, the ecology- and behavior-related adaptations of the mosquitoes delay control and make such efforts less effective, thereby contributing to the persistence of malaria in cities [56].

**Emergent properties of malaria transmission**

The small-world and scale-free properties that feature our CLD indicate that the network is resilient and the identified leverage points could help to set more adequate policy recommendations.

The functional analysis of the network allowed to identify the determinants of the more central standing for potential intervention points such as causal, impacted, closest, mediator, and influential, and derive from them key leverage points. Thus, we found that i) the *malaria positive cases* was both, the most influential and the greatest mediator; and ii) the *number of breeding sites* had the larger effects. These findings align with a recent review of malaria determinants for sub-Saharan Africa [57] that highlights the surge of infection as an intricate interplay between mosquitoes, humans, and their environments. Furthermore, i) the *drug prescription* was the closest determinant, and ii) the *householders' awareness and decision-making on malaria infection risk* the most important cause. This indicates that malaria transmission and persistence rely heavily on human behavior, which opens opportunities for more targeted policy action.

The CLD was able to disclose the interactions among malaria determinants and also permitted to track the causal links among them that preserve transmission and the feedback loops that
reinforce certain sets of determinants [58], which permits signaling emerging properties of the system post the NA [59].

Conclusions

The proposed CLD contributed to illustrate the complexity of malaria transmission and persistence in our case study, Accra, Ghana. It showed that beyond the mere biological processes and the physical environment, the behavior of people play a key role in malaria transmission and persistence. The CLD embodies three major loops that trigger and maintain transmissions in urban environments. Furthermore, the NA enabled the detection of emergent properties of the system and the identification of the key levering determinants. Besides, the topology disclosed by the CLD revealed that all leverage points need to be accounted for strategic policy development. Hence, major efforts toward preventing malaria transmission are needed, and on that, the key priorities should be: to reduce malaria persistence by reducing mosquito density, for instance, through the regular drainage of gutters or treating breeding sites with larvicides; and reducing infections by increasing the awareness of city dwellers on malaria literacy, for instance, through regular campaigns in deprived communities, both, on the field and social media. Ongoing measures, like, protecting windows and doors with mosquito-proof netting and the use of ITNs, should be intensified. Besides, an improvement of the healthcare system through regular training of the healthcare workers in malaria can enhance trust in the healthcare system and limit the risk of patients' non-compliance to malaria-drugs prescription.

Authors disclaimers

The above-mentioned findings and conclusions of this study are those of the authors and do not represent the official position of the Center for Development Research (ZEF). Besides, the findings
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**Authors contributions**

All authors fulfill the contribution requirements as per the International Committee of Medical Journal Editors’ role of authors and contributors’ guidelines. MKS: conception, data analysis, software, drafts; DCC: conception and drafts; HEZT & CB: drafts and supervision.

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**Conflicts of interest:**

The co-authors of this manuscript have any competing interests to declare

**Ethical approval**

The study was approved by the ethics committees of the Center for Development Research, the University of Bonn (Germany), and the Institute of Statistical, Social and Economic Research, University of Ghana.

**Availability of data and materials**

All relevant data are provided in the manuscript or available from published materials as cited.
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