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SORT IT: MALARIA ELIMINATION SUPPLEMENT

# Case management of malaria in Swaziland, 2011–2015: on track for elimination?

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**Objective:** To assess adherence to malaria diagnosis and treatment guidelines (2010 and 2014) in all health care facilities in Swaziland between 2011 and 2015.

**Methods:** This was a cross-sectional descriptive study involving all health care facilities that diagnosed and managed malaria cases in Swaziland. Patients' age, sex, diagnosis method and type of treatment were analysed.

**Results:** Of 1981 records for severe and uncomplicated malaria analysed, 56% of cases were uncomplicated and 14% had severe malaria. The type of malaria was not recorded for 30% of cases. Approximately 71% of cases were confirmed by rapid diagnostic tests (RDT) alone, 3% by microscopy alone and 26% by both RDT and microscopy. Of the uncomplicated cases, 93% were treated with artemether-lumefantrine (AL) alone, 5% with quinine alone and 2% with AL and quinine. Amongst the severe cases, 11% were treated with AL alone, 44% with quinine alone and 45% with AL and quinine. For severe malaria, clinics and health centres prescribed AL alone more often than hospitals (respectively 13%, 12% and 4%, $P = 0.03$).

**Conclusion:** RDTs and/or microscopy results are used at all facilities to inform treatment. Poor recording of malaria type causes difficulties in assessing the prescription of antimalarial drugs.

Despite its being a preventable and treatable illness, the burden of malaria remains high. In 2015, 96 countries had ongoing transmission and 214 million new cases were reported worldwide.[1] Of the 430 000 annual deaths reported globally in 2015, approximately 90% occurred in Africa.[1]

Between 2000 and 2015, global malaria morbidity and mortality rates fell by 37% and 60%, respectively, due in part to an expansion of malaria interventions.[1] A decrease in malaria incidence from 3.9 to 0.07 cases per 1000 population was recorded between 1999 and 2009 in Swaziland.[2] Following this decrease, the first elimination strategy was drafted in 2008, with the aim of eliminating malaria by 2015.[3] Following a World Health Organization (WHO) supported Malaria Programme Review (MPR) in 2011, and based on lessons learnt from gaps identified during the first 3 years of implementation, a new elimination strategy was developed for 2015–2020.[4] This new strategy takes an advanced and critical approach to detailing the targeted interventions and necessary systems required for Swaziland's certification of elimination and transition to prevent the re-establishment of malaria.

To achieve malaria elimination, adequate case management through the use of accessible, highly sensitive diagnostic methods that result in the rational prescription of effective antimalarial drugs is essential; this also results in positive outcomes for the individuals affected by malaria.[5–7] At community level, effective treatment leads to a reduced infectious reservoir, and prevents the emergence and spread of drug resistance.[8]

Achieving the above goals requires that health care providers adhere to diagnostic and treatment guidelines, and that patients complete their course of medication. Several studies have shown that although 70–80% of populations living in developing countries seek treatment for malaria at public and private health facilities, the quality of these health services is questionable.[9,10] These reports suggest that adequate case management at health facilities is likely to benefit the majority of patients and accelerate elimination targets.

Among countries where malaria transmission has declined, management protocols recommend that artemisinin-based combination therapies (ACTs) be used for treatment only for confirmed cases of malaria.[11] Making the correct diagnosis is crucial; doing so will reduce the waste of expensive ACTs and make the best use of donor funding. Monitoring adherence to diagnostic and treatment protocols is therefore an important element in ensuring malaria elimination. No studies have evaluated the diagnosis and treatment of malaria in Swaziland to date.

The aim of this study was to evaluate the management of confirmed malaria cases in Swaziland between January 2011 and August 2015 by evaluating adherence to the national diagnosis and treatment guidelines.

## METHODS

### *Study population*

The study included all confirmed patients treated for malaria in all health facilities of Swaziland between January 2011 and August 2015. Once a malaria case was confirmed, the facility sent a text message to the National Malaria Control Programme (NMCP), which then initiated an active case investigation. This involved the surveillance unit carrying out a case follow-up in the facility and within 1 km of the patient's

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residence in the community. The data on patient, management and treatment outcomes were then recorded in an active case-finding database that was aggregated at facility and national levels.

### Study design

This was a descriptive cross-sectional study utilising data routinely collected from the health facilities by the Swaziland NMCP.

### Study setting

#### General setting

Swaziland, a small, low-income country in southern Africa, shares borders with Mozambique and South Africa. The country has a population of 1 300 000, of whom the majority are ethnic Swazi. Approximately 70% of the population resides in rural areas. Life expectancy at birth was estimated at 49 years in 2013.[12] The country's per capita gross national product was US$3550 in 2014,[12] with agriculture the main economic activity. The country has diverse ecological zones, with climatic conditions ranging from sub-humid, cooler temperatures in the Highveld to semi-arid, warm-to-hot temperatures in the Lowveld. Malaria transmission occurs in the Lowveld, where approximately 30% of the population lives.[13] *Plasmodium falciparum* remains the predominant parasite in Swaziland, accounting for over 99% of malaria cases.[14] Transmission of malaria occurs primarily during the rainy season, between November and May.[15]

Swaziland has a total of 287 health care facilities, of which eight are hospitals, five are health centres (hospitals with minimal in-patient capacity), five are public health units and the remainder are clinics. Of the 287 facilities, 40% are owned by government, 30% by private interests, 12% by missions, 11% by industry and the remaining 7% by non-governmental organisations (NGOs). Only 14 of the 287 health care facilities have adequate capacity for performing microscopy.

### Management of malaria in Swaziland

Swaziland's strategic plan for malaria elimination, implemented in 2010, included a robust surveillance programme for prompt identification of local and imported malaria cases and for testing all persons living within a 1 km radius of a confirmed case. The strategic plan led to the revision of the country's diagnostic and treatment guidelines and the adoption of the WHO guidelines for low-transmission settings. The 2010 case management guidelines required that all cases of fever be confirmed for malaria infection by rapid diagnostic test (RDT) or microscopy before treatment is initiated. Treatment was switched from chloroquine to artemether-lumefantrine (AL) as the drug of choice for uncomplicated cases, and quinine for severe cases and as first-line treatment for pregnant women in their first trimester of pregnancy. Malaria diagnosis and treatment is currently administered in all public and private facilities according to the 2014 revised Swaziland National Malaria Diagnosis and Treatment Guidelines,[16] in which parenteral quinine was replaced by parenteral artesunate for all severe cases. Although parenteral artesunate had been procured by the NMCP, the stocks had not yet been delivered by the time this study ended. The NMCP provides all antimalarial drugs free of charge to both private and public health facilities.

### Analysis and statistics

The study variables included patient characteristics (patient identification, age, sex), method of diagnosis (RDT, microscopy, clinical), ownership of facility and facility level of diagnosis, and type of treatment. EpiData software (v. 3.1 for entry and v. 2.2.2.182 for analysis, EpiData Association, Odense, Denmark) was used for data entry and analysis. As all cases of malaria were included, no sampling was required.

### Ethical considerations

The study was cleared by the Ethics Advisory Group (EAG) of the International Union Against Tuberculosis and Lung Disease (EAG Number 53/15) and by the Scientific and Ethical Committee of the Swaziland Ministry of Health (REF: MH/599C/FWA 000 15267/IRB 9688).

## RESULTS

During the period from January 2011 to August 2015, Swaziland recorded 1981 confirmed cases of malaria (range 229–606 cases per year) of whom 71% ($n$ = 1396) were males, 12% ($n$ = 233) were children aged <5 years and 57% ($n$ = 1122) were diagnosed with uncomplicated malaria. For 30% of cases, however, type of malaria was not recorded due to poor or incomplete documentation between 2011 and 2012. AL alone was administered as the first antimalarial drug to 78% of confirmed malaria cases. The patients' demographic and clinical characteristics are shown in Table 1.

Almost all cases were diagnosed by RDT in government (98%), mission (96%) and privately owned facilities (97%), either singly or in combination with microscopy. Mission-owned facilities were more likely to use both RDT and microscopy testing (35%) than the other facilities (Table 2).

Most cases reported in hospitals were confirmed by both RDT and microscopy (59%), compared to 36% and 10% in health centres and clinics, respectively (Table 3). RDT and microscopy were carried out concurrently for quality purposes. Patients who were positive by one or both methods were prescribed antimalarial drugs. Clinics were more likely to rely on RDTs (89%) than health centres (60%) and hospitals (33%).

Overall, 5% of cases with uncomplicated malaria were treated with quinine alone, while 11% of patients with severe malaria were prescribed AL alone (Table 4). Information obtained from the NMCP surveillance unit revealed that health care facilities had experienced stock-outs of the appropriate drugs and had issued prescriptions against the recommendations of the national and treatment guidelines rather than let the patient leave without treatment, due to fears of deterioration in health or even death. There is no space for this information to be recorded or captured on the case investigation form.

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Conflicts of interest: none declared.

**TABLE 1** Demographic characteristics* of malaria patients managed in health care facilities, Swaziland, January 2011–August 2015

| Characteristic | *n* (%) |
|---|---|
| Sex | |
| Male | 1396 (71) |
| Female | 582 (29) |
| Not recorded | 3 (<1) |
| Age at diagnosis | |
| Median age, years [IQR] | 26 [11–37] |
| <5 years | 233 (12) |
| ⩾5 years | 1651 (83) |
| Not recorded | 97 (5) |
| Nationality | |
| Swazi | 1403 (71) |
| Mozambican | 528 (27) |
| South African | 11 (<1) |
| Other | 39 (2) |
| Type of malaria | |
| Uncomplicated | 1122 (57) |
| Severe | 268 (14) |
| Not recorded | 591 (30) |
| Level of facility | |
| Hospital | 504 (25) |
| Health centre | 302 (15) |
| Clinic | 1159 (59) |
| Not recorded | 16 (1) |
| Facility | |
| Government | 920 (46) |
| Mission | 722 (36) |
| Private | 317 (16) |
| Not recorded | 22 (1) |
| Method of diagnosis | |
| RDT | 1399 (71) |
| Microscopy | 60 (3) |
| RDT and microscopy | 518 (26) |
| Not recorded | 4 (<1) |
| Antimalarial drug prescribed | |
| Artemether-lumefantrine alone | 1539 (78) |
| Quinine alone | 260 (13) |
| Artemether-lumefantrine + quinine | 162 (8) |
| Other | 10 (1) |
| None | 10 (1) |

*Source: National Malaria Control Programme active case investigation database.
IQR = interquartile range; RDT = rapid diagnostic test.

**TABLE 2** Method of malaria diagnosis by ownership of health facility, Swaziland,* January 2011–August 2015

| Method of diagnosis | Government *n* (%) | Mission *n* (%) | Private *n* (%) | Unknown *n* (%) |
|---|---|---|---|---|
| RDT | 713 (78) | 438 (61) | 226 (71) | 22 (100) |
| Microscopy | 24 (3) | 29 (4) | 7 (2) | 0 |
| RDT and microscopy | 181 (20) | 254 (35) | 83 (26) | 0 |
| Unknown | 2 (<1) | 1 (<1) | 1 (<1) | 0 |
| Total | 920 | 722 | 317 | 22 |

*Source: National Malaria Control Programme active case investigation database.
RDT = rapid diagnostic test.

**TABLE 3** Type of facility* reporting malaria cases by method of diagnosis in Swaziland, January 2011–August 2015

| Method of diagnosis | Hospital *n* (%) | Health centre *n* (%) | Clinic *n* (%) | Unknown *n* (%) | Total *n* (%) |
|---|---|---|---|---|---|
| RDT | 165 (33) | 181 (60) | 1037 (89) | 16 (100) | 1399 |
| Microscopy | 44 (9) | 10 (3) | 6 (1) | 0 | 0 |
| RDT and microscopy | 295 (59) | 109 (36) | 114 (10) | 0 | 518 |
| Not recorded | 0 | 2 (<1) | 2 (<1) | 0 | 4 |
| Total | 504 | 302 | 1159 | 16 | 1981 |

*Source: National Malaria Control Programme active case investigation database.
RDT = rapid diagnostic test.

**TABLE 4** Type of antimalarial drug prescribed by severity of confirmed malaria, Swaziland, January 2011–August 2015*

| Drug prescribed<br>Malaria severity | AL *n* (%) | QN *n* (%) | AL+QN *n* (%) | Other *n* (%) | Total *n* (%) |
|---|---|---|---|---|---|
| Uncomplicated | 1035 (93) | 52 (5) | 21 (2) | 6 (<1) | 1114 (100) |
| Severe | 30 (11) | 117 (44) | 119 (45) | 1(<1) | 267 (100) |
| Total | 1065 (77) | 169 (12) | 140 (10) | 7 (<1) | |

*Source: National Malaria Control Programme active case investigation database.
AL = artemether-lumefantrine; QN = quinine.

Further analysis indicated that more cases with severe malaria were prescribed AL alone in government-owned facilities (19%, 16/86 cases) compared to missions (8%, 12/159 cases) and private clinics (9%, 2/22 cases). Clinics and health centres tended to prescribe AL alone more often for severe malaria, compared to hospitals (13%, 4/32, 12%, 6/50 and 4%, 7/186, respectively).

## DISCUSSION

This is the first study of malaria case management undertaken in Swaziland, approximately 5 years after the policy shift from clinical diagnosis and treatment of uncomplicated malaria with chloroquine to the use of ACT to treat confirmed cases only. These results provide a snapshot of the implementation of the national malaria diagnosis and treatment guidelines, and provide the NMCP with valuable information on areas that require improvement for the new policies to have a real impact on malaria control and elimination. Adequate management of malaria cases involves ensuring that all febrile illnesses are diagnosed by RDT or microscopy, and that both methods are quality assured. Only patients with positive RDT or microscopy results should be prescribed antimalarial drugs: AL for uncomplicated malaria and quinine for severe malaria and/or pregnant woman. The prescribing health care staff must take into account the patients' weight, age and malaria type to guide treatment.

During the study period several standardised health worker training sessions were conducted, aimed at familiarising health workers with the new guidelines and further incorporating them into practice. The findings revealed that the majority of malaria cases were confirmed by RDTs in all health facilities, and less frequently by microscopy. Between July 2011 and June 2012, 64% of febrile illnesses were confirmed by RDT, 13% by microscopy and 23% by both RDT and microscopy.[17] The findings in the present study show that almost all febrile illnesses were confirmed by either RDT or microscopy or both, suggesting an improvement in adherence to the country guidelines. These findings are consis-

tent with reports from Zambia 1 year after the introduction of RDT and AL treatment.[18] Clinics and health centres tended to rely more on RDT, while hospitals, which were more likely to have laboratories, used microscopy in addition to RDT.

At low rates of endemicity, low parasite density infections are not only more common, they are also very difficult to detect, hence the WHO's recommendation to use RDTs and microscopy. Microscopy also has the advantage of quantifying malaria parasites and identifying the infecting species. Quality assurance for microscopy is, however, operationally challenging and labour intensive, particularly in low transmission settings. The WHO therefore recommends increasing the use of both methods where possible. Standardised protocols for the quality assurance of RDTs, particularly to verify large numbers of negative results, are currently not available. While molecular diagnostic tools based on nucleic acid amplification (polymerase chain reaction and loop-mediated isothermal amplification) would offer maximum benefit, large-scale implementation of these techniques poses several challenges in the management of malaria cases. The proportion of suspected malaria cases receiving a parasitological diagnosis (RDT, microscopy or both) has nonetheless increased markedly since 2010, when RDTs and ACTs were first introduced. Adherence to diagnosis and treatment guidelines for malaria management is considered a cost-effective intervention; a study conducted in Kenya demonstrated that correct management of malaria can save up to 60% of costs associated with malaria treatment.[19]

Several studies have found that cost, patient preference and the availability of drugs and diagnostics all influence provider adherence to case management guidelines.[20,21] In this study, the NMCP provided diagnostic and antimalarial drugs free of charge, along with provider training.

Almost two thirds of the confirmed malaria cases in Swaziland were uncomplicated, and most were treated with AL, while severe malaria was commonly treated with quinine. Disturbingly, some cases of uncomplicated malaria were treated with quinine, while some patients with severe malaria were treated with AL, in contradiction with recommendations in the national treatment guidelines. Prescriptions of AL for severe malaria could result in deterioration of the patient's health status or even death. The reported inappropriate prescription of AL for severe cases and quinine for uncomplicated malaria is in line with reports of inappropriate prescription of antimalarial drugs by health care providers following implementation of national guidelines in other African countries.[22–24] Several factors responsible for the non-adherence of clinic staff to the recommended guidelines have been cited among sub-Saharan countries. These include inadequate supplies of the recommended drugs[25] and inadequate training of the prescribers.[26,27] An in-depth understanding of all these issues is essential for the generation of information to improve malaria case management in Swaziland.

One strength of this study was that it analysed all cases from all health facilities in the country. It is possible that patients did not seek medical attention from health facilities due to perceived costs, but this is likely to represent a small number of patients, as RDTs and malaria treatment drugs are provided free of charge to all health facilities. Furthermore, most major fields in the database were completed, apart from malaria type, which was recorded only from 2012.

There were some limitations in the study. There were gaps in the database used for the analysis. Quality of medical records is a major limiting factor when conducting retrospective studies; similar limitations have been reported elsewhere.[28] Data on clinically treated cases of malaria were not available because the database was derived from active case investigations conducted after reports of a confirmed case. Furthermore, the pregnancy status of some of the female cases was not recorded and the reasons for this were not provided. Knowledge of the correct drug and dosage for each pregnancy trimester and adherence to the correct dosage among prescribing health care personnel is important. Incorrect or sub-optimal treatment of malaria among pregnant women can adversely affect the mother and foetus, resulting in maternal anaemia, foetal loss, intrauterine growth retardation, premature delivery or low birth weight with increased risk of neonatal death.[29] Studies in Uganda and Kenya reported contraindicated malaria regimens prescribed for first-trimester women.[30,31] Swaziland recently added 0.25 mg/kg body weight primaquine with ACT for non-pregnant women and adults to the treatment guidelines to reduce the transmission of malaria parasites to the mosquito vector. As this addition was made only recently, in 2014, adherence to primaquine was not assessed.

The study has a number of programmatic implications. First, use of both RDT and microscopy to confirm malaria cases should be increased, in accordance with WHO guidelines for low-transmission settings. Use of both RDT and microscopy has the advantage of identifying low parasite density and facilitating treatment of possible carriers who may fail to be identified by a single method. Second, the NMCP should also conduct training to specifically improve the recording and management of vulnerable patients (i.e., pregnant women and children aged <5 years). The correct dosing and choice of drugs for pregnant women needs to be understood by clinical staff. Child formulations of AL are not available in Swaziland, and this is likely to be an influencing factor in the failure to record vulnerability status. Third, although the results of the study are encouraging, the gaps in the programme require attention. Operational research is required to clearly understand treatment practices, attitudes and other influencing factors among health care staff. We were unable to address these crucial factors in the study. Additional efforts are required to optimise passive case detection and the promotion of appropriate health-seeking behaviour to reduce parasite sources that promote transmission.

## CONCLUSION

This study of malaria case management in Swaziland showed encouraging results and detected some areas for improvement. Adequate recording of pregnancy status and provision of child-friendly formulations for treatment will improve the performance of Swaziland's malaria programme and accelerate the country's progress towards the goal of eliminating malaria. Increased use of RDTs alone, and reduced duplication with microscopy when an RDT is positive, should free up laboratory resources, and attention should be focused on correct treatment for uncomplicated and severe malaria. Regular quality control of both RDTs and microscopy, however, has the advantage of providing a reliable diagnostic result and ensuring appropriate prescription.

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**Objectif :** Evaluer l'adhérence aux directives de diagnostic et de traitement du paludisme (2010 et 2014) dans toutes les structures de santé du Swaziland entre 2011 et 2015.
**Méthodes :** Une étude transversale descriptive impliquant toutes les structures de santé qui ont diagnostiqué et pris en charge des cas de paludisme au Swaziland, a été réalisée. On a analysé l'âge des patients, leur sexe, la méthode de diagnostic et le type de traitement.
**Résultats :** De 1981 dossiers de paludisme grave et non compliqué analysés, 56% de ces cas ont été non compliqués et 14% ont été graves. Le type de paludisme n'a pas été enregistré dans 30% des cas. Près de 71% des cas ont été confirmés par des tests de diagnostic rapide (RDT) seuls, 3% par microscopie seule et 26% par RDT et microscopie à la fois. Parmi les cas non compliqués, 93% ont été traités par l'artéméther-luméfantrine (AL) seul, 5% par quinine seule et 2% par AL et quinine. Parmi les cas graves, 11% ont été traités par AL seul, 44% par quinine seule et 45% par AL et quinine. Les dispensaires et les centres de santé prescrivent plus souvent l'AL seul en cas de paludisme grave, comparés aux hôpitaux (respectivement 13%, 12% et 4% ; $P = 0,03$).
**Conclusion :** Les résultats de RDT et/ou de microscopie sont utilisés dans toutes les structures pour guider le traitement. Un enregistrement médiocre du type de paludisme crée des difficultés pour évaluer la prescription des médicaments antipaludéens.

**Objetivo:** Evaluar el cumplimiento de las orientaciones en materia de diagnóstico y tratamiento del paludismo (2010 y 2014) en todos los establecimientos de salud de Swazilandia del 2011 al 2015.
**Métodos:** Un estudio transversal descriptivo de todos los centros de atención de salud que diagnostican y tratan casos de paludismo en el país. Se analizó la edad de los pacientes, el sexo, el método diagnóstico y el tipo de tratamiento antipalúdico.
**Resultados:** Se analizaron 1981 historias clínicas de casos de paludismo grave y sin complicaciones; el 56% de estos casos no presentó complicaciones y el 14% correspondió a casos de paludismo grave. El tipo de paludismo no se registró en el 30% de los casos. Alrededor del 71% de casos se confirmó solo mediante pruebas diagnósticas rápidas (RDT), el 3% solo por microscopia y el 26% por ambos métodos. El 93% de los casos no complicados se trató exclusivamente con la combinación artemetero + lumefantrina (AL), el 5% con quinina exclusiva y el 2% con AL y quinina. De los casos graves, el 11% se trató solo con AL, el 44% solo con quinina y el 45% con AL y quinina. En los casos de paludismo grave se receta de manera exclusiva AL, con mayor frecuencia en los consultorios y los centros de salud que en los hospitales (13%, 12% y 4% respectivamente; $P = 0,03$).
**Conclusión:** Los resultados de las RDTs o de la microscopia se utilizan en todos los establecimientos con el fin de fundamentar el tratamiento. Un registro deficiente del tipo de paludismo dificulta la evaluación de las prácticas de recetas de fármacos antipalúdicos.

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