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Research Article

# EPIWATCH®: A Rapid Epidemic Surveillance Tool for Detecting Early Signals of the First-ever Marburg Virus Outbreak in Equatorial Guinea

Pan Zhang[1], Aye Moa[1], Ashley Quigley[1]

[1]Biosecurity Program, Kirby Institute, Faculty of Medicine, University of New South Wales (UNSW)

## Abstract

Background: On February 13, 2023, Equatorial Guinea identified the Marburg virus for the first time, leading to the declaration of a Marburg virus disease (MVD) outbreak, characterized by a high fatality rate. EPIWATCH® is a rapid surveillance tool that employs artificial intelligence (AI) to detect early signals of outbreaks and the emergence of infectious diseases in real time.
Aims: This study aimed to use EPIWATCH® to identify early warning indicators of MVD in Equatorial Guinea during the three months before its official declaration by the World Health Organization (WHO) and local health authorities. Additionally, it sought to examine reported syndromes across regional Africa during the same period to explore potential signals of MVD from the neighboring countries.
Methods: We conducted a retrospective analysis using EPIWATCH® to collect syndromic surveillance data from November 2022 to February 2023 in Equatorial Guinea and across Sub-Saharan Africa.
Results: There was a notable absence of EPIWATCH® reports regarding Equatorial Guinea in the three months preceding the official declaration of the MVD outbreak, from November 2022 to early February 2023. Additionally, EPIWATCH® reports from neighboring countries did not reveal any syndromic signals of MVD across other regions of Africa during this timeframe. However, a report documenting the syndrome “hemorrhagic fever” in Equatorial Guinea was identified on February 10, 2023, before the diagnosis of the first case on February 12, 2023, serving as the early signal of the 2023 MVD outbreak.
Conclusion: The absence of early warning indicators in Equatorial Guinea and across Sub-Saharan Africa in the three months leading up to the official declaration of the outbreak remained unknown. Additional investigations, such as genome analysis or phylogenetic studies, may be required to investigate the outbreak's emergence. AI-based surveillance tools like EPIWATCH® could supplement traditional public health surveillance methods in detecting a wide range of infectious diseases worldwide.

**Keywords:** Equatorial Guinea, Marburg virus disease, MVD, hemorrhagic fever, outbreak, surveillance, early signal

## Introduction

Equatorial Guinea officially declared its first-ever Marburg virus disease (MVD) outbreak on February 13, 2023 [1]. Preceding this declaration, the deaths of at least 8 individuals in the eastern Kie Ntem province between January 7 and February 7, 2023, prompted initial investigations. These individuals exhibited symptoms such as fever, vomiting, diarrhea with blood clots, and skin lesions. On February 12, 2023, laboratory tests confirmed the presence of viral hemorrhagic fever, subsequently confirming MVD [2]. The World Health Organization (WHO) deployed field experts to assist with the national response in Equatorial Guinea, focusing on contact tracing and isolation of infected individuals. As of June 7, 2023, 23 probable and 17 confirmed cases were reported, demonstrating a high case fatality rate of 87%. Following two consecutive incubation periods (42 days) without new confirmed cases, the country declared the end of the MVD outbreak on June 8, 2023 [2].

MVD outbreaks have continued in Africa, with cases reported across various countries over the past two decades [2]. While the virus was not unfamiliar to the region, the 2023 outbreak was the first documented instance of MVD in Equatorial Guinea. Given its severity and occurrence amidst the coronavirus disease 2019 (COVID-19) pandemic, investigating the emergence of this outbreak was imperative, as it posed a significant public health challenge. Early detection of MVD signals during the 2023 outbreak in Equatorial Guinea was essential to enhance existing response strategies and inform future preparedness efforts for recurrence.

The clinical characteristics and transmission risks of MVD closely resemble those of Ebola virus disease (EVD). Early transmission likely occurs from bats or another intermediary host to humans, but the exact pathway and specific biological fluids involved remain uncertain. Infection can occur through direct contact with infected individuals' blood or bodily fluids [3]. The incubation period of MVD spans from 3 to 21 days, averaging between 5 to 10 days [4]. Following this period, patients typically present with sudden illness and a range of symptoms, including fever, vomiting, diarrhea, and rash [5]. MVD is known for its high case fatality rate (CFR), with reports indicating it to be as high as 90%. Due to clinical similarities with more widespread infections such as EVD, malaria, typhoid, or cholera, early instances of MVD are frequently missed [5].

Surveillance during the 2023 MVD outbreak in Equatorial Guinea included a WHO-supported alert system and training initiatives, aimed at strengthening case identification, contact tracing, and supervision of field professionals [2]. Despite the effectiveness of these traditional surveillance methods, concerns often exist regarding the substantial setup cost and exposure risks for personnel involved in surveillance activities. Moreover, delays between symptom onset and laboratory-confirmed diagnosis may hinder the timely detection of diseases [6].

Utilizing an open-source artificial intelligence (AI)-based system for epidemic surveillance serves as a valuable complement to traditional surveillance strategies. A diverse range of publicly accessible data, such as news reports, social media, publications, and health alerts, reflects public vigilance and discourse, as well as clinical signs and symptoms (syndromes) of the disease before formal diagnosis. AI technology can efficiently harness, curate, and analyze this information to deliver early warning indicators of epidemics much more rapidly than traditional surveillance [6].

EPIWATCH®, a curated observatory for epidemic intelligence, systematically collects global infectious disease data from various open sources in multiple languages [7]. The observatory employs AI methodologies integrating modern natural language processing (NLP) and named entity recognition (NER) algorithms to identify data points with scanned articles autonomously [6]. It generates automated reports highlighting essential elements to detect epidemic signals, including outcomes, geographic locations, timing, and situational details. These reports subsequently undergo rigorous review by analysts and epidemiologists to ensure accuracy and relevance. This tool is designed to significantly improve the detection, screening, and investigation of infectious diseases. Employing AI technology, EPIWATCH® identifies clinical syndromes indicative of potential new and emerging infectious diseases [6]. Our study aimed to use an open-source AI-based surveillance tool, EPIWATCH® to detect early signals of MVD in Equatorial Guinea during the three months before its official declaration of an MVD outbreak on February 13, 2023. Additionally, we sought to examine reported syndromes in neighboring countries across regional Africa within the same timeframe to identify potential early signals of MVD.

## Methods

We conducted a retrospective review of syndromic surveillance data from EPIWATCH® spanning from November 1, 2022, to February 13, 2023, before the declaration of the MVD outbreak in Equatorial Guinea. This three-month timeframe was selected to align with the typical progression of infectious diseases, starting with the pathogens present in the host during the incubation period and ending with transmission [5]. To identify potential MVD signals in Equatorial Guinea, we searched EPIWATCH® using a set of relevant syndromic keywords, including "hemorrhagic fever", "vomiting", "diarrhea", "fatigue", "bleeding", "febrile syndrome", "acute fever and rash", "acute gastroenteritis", and specific to the country "Equatorial Guinea". Articles that did not report syndromes or reported syndromes diagnosed with diseases in Equatorial Guinea were excluded from the study.

Additionally, to explore potential signals of MVD in neighboring countries across regional Africa, we utilized the same syndromic keyword set as listed above in EPIWATCH® along with "Sub-Saharan Africa" to retrieve reports during the same period. Syndromes reported with diagnoses other than MVD or referencing Equatorial Guinea and regions outside of Sub-Saharan Africa were excluded from the study.

Notably, in conducting this study to detect early signals of the 2023 MVD outbreak in Equatorial Guinea, our methodology primarily relied on syndromic surveillance through EPIWATCH®. However, it did not include phylogenetic analysis or genomic sequencing of the virus.

## Results

Between November 1, 2022, and February 13, 2023, EPIWATCH® captured 54 reports, aimed at identifying signals of MVD within Equatorial Guinea. Among these reports, no duplicates were identified; however, 31 reports were removed based on exclusion criteria, leaving 23 unique reports included in the study (Figure 1).

Figure 2 illustrates a notable lack of EPIWATCH® reports concerning Equatorial Guinea in the three months preceding the official declaration of MVD. Reporting in EPIWATCH® commenced on February 10, 2023, three days before the formal MVD declaration. On February 10, a single report was identified, highlighting "hemorrhagic fever". Further examination revealed that it documented the earliest cluster of fatalities in Equatorial Guinea between January and February 2023, exhibiting symptoms of "hemorrhagic fever". EPIWATCH® flagged an additional 12 reports (43%) on February 11, 2023, and 6 reports (24%) on February 12, 2023, revealing "hemorrhagic fever" as a syndrome. Notably, 4 reports

(19%) captured on February 12, 2023, were categorized as "febrile syndrome", despite the patients exhibiting symptoms of hemorrhagic fever. On February 12, 2023, a blood sample from a contact returned positive for MVD, thus confirming the initial case of MVD in the outbreak [2].

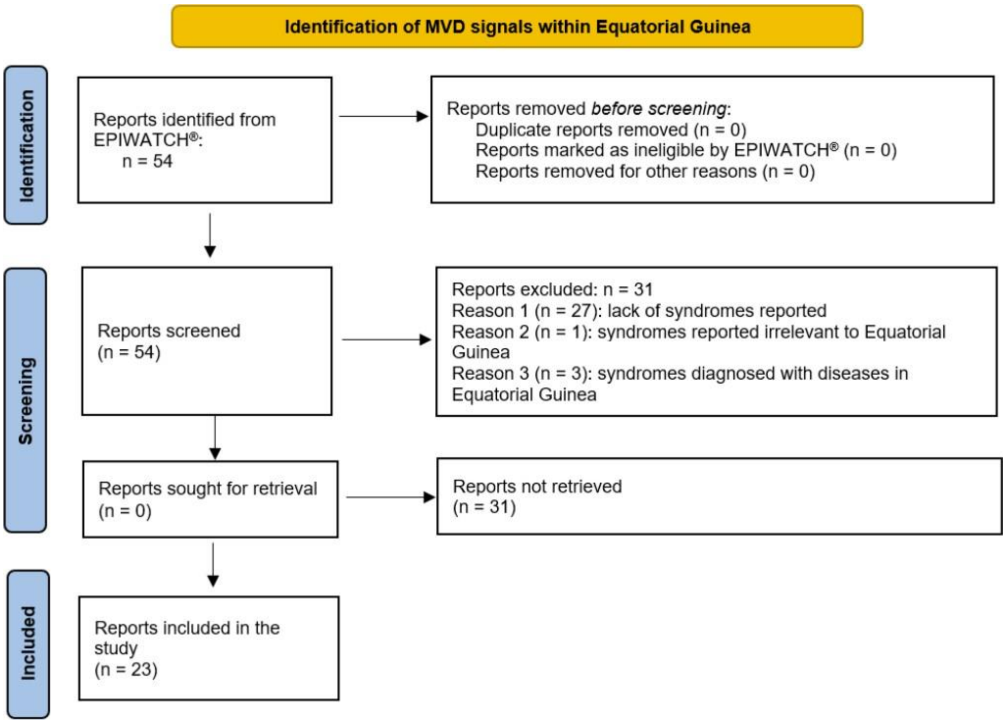

**Figure 1:** Flow Diagram of EPIWATCH® Report Selection for Identifying MVD Signals within Equatorial Guinea

During the same period, while investigating early signals of MVD in neighboring countries, EPIWATCH® identified 414 reports of syndromes across Sub-Saharan Africa. No duplicates were found; however, after examination, 391 reports were excluded as they described syndromes with diagnoses other than MVD. Among the remaining 23 reports with relevant syndromes, as shown in Figure 3, one was labeled as “hemorrhagic fever”. A subsequent investigation of the report revealed no specific regional details other than mentioning “Sub-Saharan Africa”.

## Discussion

Before the identification of the initial cluster of fatalities in the Kie Ntem province of Equatorial Guinea, EPIWATCH® had not documented any syndromes relevant to the MVD in the country between January and February 2023. The origins of the outbreak, which led to the first recorded case of MVD in Equatorial Guinea, remained unclear. In Equatorial Guinea, out of the eight provinces, confirmed or probable cases were reported in five districts across four provinces. The district most affected was Bata, located in Litoral province, which borders Cameroon [8]. Many cases were linked to shared social networks or geographic proximity. However, the presence of early clusters in several districts without clear epidemiological connections suggests there may have been undetected transmission of the virus [8]. The lack of information on travel histories and contact details for potentially infected individuals or animals associated with these initial deaths hinders efforts to identify the source of the outbreak.

While the timeframe between those early fatalities and confirming the first MVD case aligns with the typical MVD incubation period [5], our review of reported syndromes across Sub-Saharan Africa from November to February 2023 found no indicators predicting the emergence of MVD in the region. Although symptoms of MVD can closely resemble those of Ebola virus disease (EVD), cholera, and Lassa fever [9], individuals exhibiting such symptoms were diagnosed with diseases other than MVD in various regions of Africa. Nevertheless, it remains uncertain whether there were undiagnosed cases of MVD across regional Africa during the three months before Equatorial Guinea confirmed its first-ever MVD outbreak, due to the similarities with other diseases.

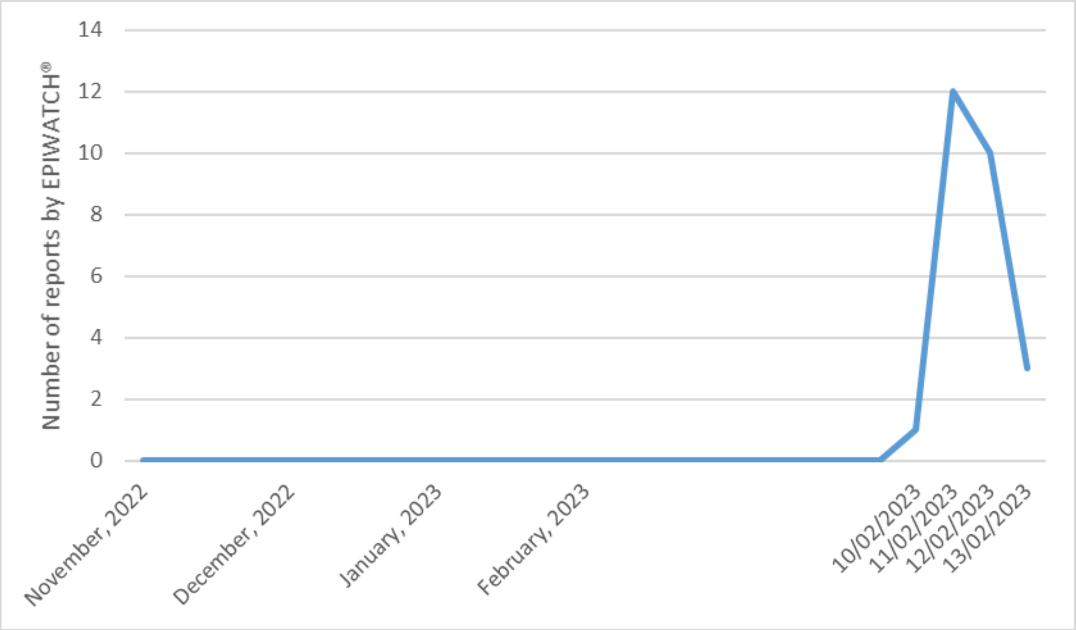

**Figure 2:** Reports captured by EPIWATCH®, Equatorial Guinea, November 2022 - February 13, 2023 (2,7)

**Footnotes:**

1. A cluster of at least 8 fatalities was identified in Kie Ntem province from January 7 to February 7, 2023; tests from contacts returned negative for MVD on February 9, 2023.
2. EPIWATCH® flagged a report of early hemorrhagic fever fatalities in Equatorial Guinea on February 10, 2023.
3. One test returned positive for MVD on February 12, 2023; Equatorial Guinea declared its first-ever MVD outbreak on February 13, 2023.

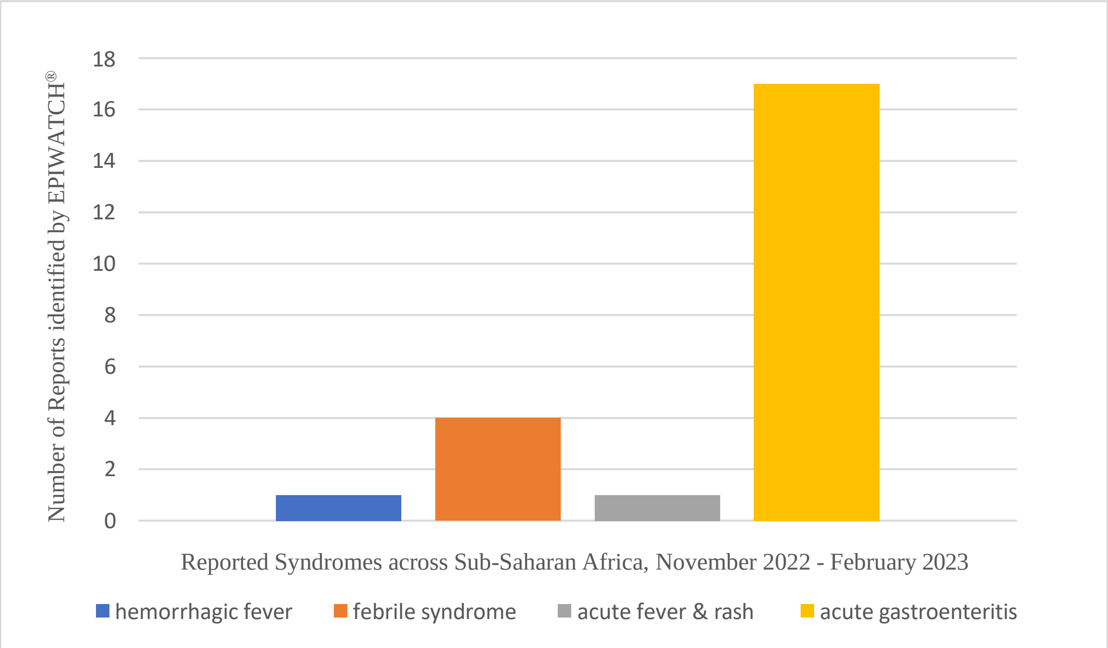

**Figure 3:** Syndromic Surveillance of MVD across Sub-Saharan Africa, Reports generated by EPIWATCH®, November 2022 - February 2023 (7)

The most recent MVD outbreak before the 2023 event in Equatorial Guinea took place in Ghana between July and September 2022. Despite the absence of a close geographical border between Ghana and Equatorial Guinea, there was no evidence indicating a direct link between these two outbreaks

[10]. However, the possibility of undiagnosed MVD cases in the African region following the 2022 outbreak in Ghana remains uncertain, potentially impacting the emergence of the Equatorial Guinea outbreak in early 2023.

MVD is a zoonotic illness that can be transmitted from bats to humans through extended exposure to habitats and body fluids of infected bats, as well as contaminated fruits. The virus was isolated from a fruit bat, Rousettus aegyptiacus, causing infections in patients across various regions of Africa between 2005 and 2008 [11]. Additionally, a 2019 study indicated that Marburg virus genomes obtained from fruit bats captured in Zambia in September 2018 were closely related to those responsible for previous outbreaks in the Democratic Republic of the Congo (DRC) [12]. A comprehensive investigation involving genomic analysis or phylogenetic study of the Marburg virus may therefore be necessary to provide further details causing the initial deaths in Kie Ntem province of Equatorial Guinea. Such efforts could contribute to understanding the origins of the MVD outbreak in Equatorial Guinea, which has occurred for the first time.

Laboratory tests confirming the initial case of MVD were completed on February 12, 2023, following the discovery of those earliest fatalities occurring between January 7 and February 7, 2023. Our finding reveals that EPIWATCH® successfully identified a report of "hemorrhagic fever" on February 10, 2023, before the formal diagnosis of the first case, thus serving as an early signal of the 2023 MVD outbreak in Equatorial Guinea. The finding underscores the ability of EPIWATCH®, an AI-driven surveillance tool, to detect infectious diseases more rapidly than traditional surveillance strategies.

Traditional public health surveillance heavily relies on human resources for sample collection and infection reporting but faces challenges, particularly in low-income countries where samples might be transported to distant laboratories, sometimes across borders [13]. AI-enabled surveillance overcomes these limitations with machine-learning algorithms, enhancing precise localization and data analysis for early infectious disease detection [14-16]. AI also offers diverse modeling techniques for simulating disease transmission and control scenarios. Models including support vector machine (SVM), gradient boosting machine, and random forests (RF) were used to predict global mosquito-borne disease spread, such as Zika virus and dengue [16-18]. RF assessed dengue transmission risk in Singapore using comprehensive data sets [16]. These AI techniques facilitate context-specific prediction, risk stratification, and evaluation of control strategies under varied environmental conditions [19-20]. However, it is crucial to emphasize that AI-based surveillance methods complement rather than replace traditional strategies, particularly in understanding outbreak origins [6]. Integrating AI-driven surveillance tools such as EPIWATCH®, enhances disease tracking and early warning capabilities within established public health surveillance systems.

This study was not without limitations. There was a risk of overlooking signals in our surveillance of outbreak syndromes, potentially due to insufficient local reporting. Furthermore, AI-based surveillance systems exhibited inherent imperfections, leading to false alarms or the omission of significant epidemiological signals. Therefore, continuous recalibration based on emerging data is crucial for identifying early warning indicators of epidemics [6]. Nonetheless, despite these limitations, the study highlights the effectiveness of EPIWATCH® in detecting early signals of the 2023 MVD outbreak in Equatorial Guinea.

## Conclusion

This study examined early indicators of the first Marburg virus disease outbreak in Equatorial Guinea over the three months preceding the official outbreak declaration, employing the rapid epidemic surveillance tool EPIWATCH®. It also examined reported syndromes across Sub-Saharan Africa during the same period to identify early Marburg virus disease signals. Powered by artificial intelligence, EPIWATCH® successfully flagged a report describing a "hemorrhagic fever" syndrome on February 10, 2023, as an early signal, preceding the diagnosis of the first case. Artificial Intelligence-based epidemic surveillance tools, such as EPIWATCH®, should be utilized to complement traditional surveillance strategies for detecting epidemic signals and monitoring various infectious disease outbreaks.

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## Data Availability Statement

All data is publicly available.

## Ethics

Ethics approval and informed consent were not required for this study because it did not involve human or animal subjects. All data used was publicly available and anonymous.

## Author Contributions

PZ contributed to the conception of the study, study design, data collection, data interpretation and analysis, original manuscript drafting, and revision. AM contributed to the conception of the study, study design, manuscript revision, and review. AQ contributed to the conception of the study, study design, manuscript revision, and review.

## Declarations of Interest

All authors stated that there are no conflicts of interest to declare for this study.

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