

Diagnostic and Treatment Strategies for Acute Febrile Illnesses (AFIs)

Ajay Undrakonda, Terry Oroszi

Department of Pharmacology & Toxicology, Boonshoft School of Medicine, Wright State University, Fairborn, OH, USA

Email: terry.oroszi@wright.edu

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Abstract

Acute fever is common in the tropics, presenting as chills, headache, muscle and joint discomfort. High temperatures usually subside independently but may indicate severe illness. The review addresses the epidemiology, etiology, and treatment of acute febrile illnesses (AFIs). In many countries, the infectious etiology and epidemiology of AFI, a disease lasting at least a week with no recognized cause, are poorly understood. Sentinel hospital studies in Sub-Saharan Africa and Southeast Asia track AFI cases, collect clinical and public health data, and identify susceptibility patterns. Dengue fever and leptospirosis are significant in tropical areas but challenging to quantify. AFI can be classified as nonmalarial, diagnosed, or undiagnosed, depending on the suspected cause. Treatment should consider the patient's specific circumstances and fever severity. Most patients see symptoms disappear within two to three weeks of treatment. Antimalarial, antibiotic, and antiviral medications should be taken with food, as directed by a doctor. Multivitamins may help with extreme fatigue, dizziness, nausea, vomiting, or headaches. In the tropics and subtropics, antimalarial drugs have traditionally been used for high fevers due to the common belief that malaria is the cause. However, most fever cases have other causes. A comprehensive approach to treating acute febrile syndrome (AFS) must include knowledge of various diseases, innovative diagnostic and therapeutic tools, and long-term treatment algorithms. The limited availability of point-of-care diagnostics in low-resource settings is a major challenge—one that can be addressed with minimal effort and cost if preventative measures are taken. Developing simple, inexpensive, and accurate diagnostic methods could significantly advance public health in these regions by enabling rapid identification and treatment of the specific causes of AFIs, leading to improved patient outcomes and reduced disease burden.

Keywords

Acute Febrile Illnesses, Epidemiology, Diagnosis, Treatment, Nonmalarial

1. Introduction

Acute febrile illness (AFI), often called acute fever (AF) or short febrile illness (SFI), is medically defined as a fever that subsides on its own within three weeks or, at most, within two weeks. Due to the lack of understanding of what triggers acute febrile illness, medical professionals from different parts of the world have been unable to settle on a single definition. However, fevers above the normal range of 98.6 degrees Fahrenheit or 37 degrees Celsius can be traced back to identifiable causes and can lead to severe febrile disease. One possible factor in the propagation of an epidemic is a shift in a country's climate or weather patterns. Malaria, scrub typhus, rickettsial fevers, dengue fever, leptospirosis, and flu are only a few viruses, bacteria, protozoa, and rickettsia that can cause AFI. Despite their identification, it is not always obvious what causes the patient's AFI symptoms. An acute febrile illness (AFI) can be classified as nonmalarial (AFI nonmalarial), diagnosed (Diagnosed AFI), or undiagnosed (AFI undiagnosed), depending on the suspected cause of the fever [1].

It is crucial to understand how AFI develops in people and to provide the right medical care to ensure rapid recovery given the prevalence of AFI, especially in tropical countries such as India during the monsoons and during intercalary times between the seasons. Medical experts frequently misdiagnose AFI as a common cold, viral fever, or even malaria [2]. Acute febrile infections are characterized by a high core body temperature that does not return to normal after four days of therapy with the standard course of antibiotics or antiviral drugs, according to the medical community's consensus. Other characterizations include skin irritation, disease (typhoid, jaundice, bleeding), muscle and joint pain (arthritis), and fatigue. There can be multiple etiologies for fever, so it can take many tests to determine if a patient has an acute febrile illness (AFI). Examining the margin of the smear is an important diagnostic test that works with the patient's physical exam and medical history to make the right diagnosis. When analyzing a blood sample, doctors look at the number, type, and size of the patient's red blood cells, white blood cells, and platelets under the microscope [3].

In a quick diagnostic test (QDT), a single drop of the patient's blood is collected using a sterile needle and then spotted onto an antigen plate for examination (RDT). Antigens (proteins) for malaria, dengue fever, jaundice, typhoid, and other prevalent tropical diseases are shown on the plate. If the antigen on the plate has bound to the blood sample, we can see it under the microscope. A simple lab test can tell if the patient has been exposed to a virus or bacterium that causes malaria, dengue, jaundice, or typhoid [4].

The enzyme-linked immunosorbent assay (ELISA) is a biochemical test that uses a patient's blood sample to find an antigen (binding agent) by using an antibody

as a ligand. Proteins called antigens can be found on the surface of disease-causing bacteria and viruses. Often used to identify rickettsial diseases and leptospirosis, the ELISA test has gained widespread use in recent years [5].

A detailed blood sample analysis may be performed by polymerase chain reaction (PCR), which amplifies DNA from blood samples and then compares the resulting signal with that of a healthy person and the DNA of the causative microbiological pathogen. In the case of AFI, a positive diagnosis can be made if the patient's DNA signal matches exactly that of the invading bacteria [6].

Treatment for AFI should be initiated by a medical professional who considers the individual patient's circumstances and the severity of their fevers. Once therapy has begun, most patients have a complete cure for fever symptoms in two to three weeks. Antimalarial, antibiotic, and antiviral medications should be taken with food, as directed by the physician. For symptoms like fatigue, dizziness, nausea, vomiting, or headache, taking a multivitamin can help [7].

2. Clinical Signs and Differential Diagnosis of Acute Febrile Illness

The first major studies were written to provide clues for diagnosis and treatment. If the primary tests do not help narrow down a possible diagnosis, move on to the blood culture sensitivity and urine culture sensitivity. In other cases, the symptoms of the illness are mild, the clinical course is brief, and the patient fully recovers within a few days. The presence may inform a preliminary diagnosis and the main therapy of elevated white blood cell counts and thrombocytopenia. They used various diagnostic tools, including the dengue fever test, the Wimal test, the malaria card, and the chest radiograph, to identify cases of viral fever during the summer and fall. A urine culture and sensitivity test were submitted since urinary tract infections are one of the leading causes of fever in women. As sepsis and other blood-related infections can cause persistent fevers, blood cultures, and sensitivity were used to determine the causative organism and potential therapy field [8].

The clinical presentation of this disease ranges from a minor infection to a life-threatening illness defined by the breakdown of several organ systems. The patients showed similar clinical symptoms to those described in an Indian study [9].

Medically proven fever is acute unilateral fever (AUF), while undiagnosed fever is unilateral fever (UUF). Interleukin I (IL-1), IL-6, and other endogenous pyrogens, including tumor necrosis factor-alpha, have been implicated in the pathogenesis of FUO (TNF-alpha). Even for experienced doctors, acute undifferentiated febrile illness can be challenging to identify and treat. In cases of rheumatoid arthritis and systemic-onset juvenile rheumatoid arthritis (JRA) [Still disease], individuals have had a fever of unknown origin (FUO). Crohn's disease continues to be the most common cause of FUO in the gastrointestinal system today. Those with FUO related to typhoid or TB were more likely to have a continuous fever pattern than those with connective tissue diseases [10].

Compared to vivax malaria and mixed infections, Falciparum malaria was associated with a much lower average number of platelets and a higher risk of bleeding. The results of this study are consistent with their findings. Hospitalizations for tropical fever accounted for 8% of all admissions to the ICU. Unfortunately, research mostly focuses on discrete infections such as dengue, malaria, and scrub typhus; thus, neither the profile nor the proportion of differential diagnosis for undifferentiated febrile disorders is well represented. Viruses are responsible for fever and certain influenza-like diseases [with a mild sore throat and cough]. When upper respiratory symptoms are accompanied by systemic symptoms such as fever and malaise, we consider it an influenza-like illness. High fever has persisted for at least three to four days, particularly with facial pain or nasal discharge [11].

Scrub typhus and murine typhus can cause maculopapular rashes, eschars on the skin, and lymphadenopathy in the regional lymph nodes. Scrub typhus usually causes problems with the respiratory system, acute renal failure, vomiting, and loose stools. It can also cause conjunctival suffusion, muscle pain, and jaundice [12]. If a person has a high body temperature, stomach symptoms, and an enlarged spleen that continues for more than a few days, they may have typhoid. Tuberculosis testing should be done on patients with prolonged undisclosed fevers, particularly on those who have also lost weight. Petechiae, subconjunctival hemorrhages, ecchymoses, and a positive tourniquet test can indicate bleeding in individuals with severe dengue fever [13].

3. Malaria and Nonmalarial Febrile Illnesses (NMFI)

In the tropics and subtropics, doctors have traditionally used antimalarial drugs to treat high fevers because most people think that malaria is to blame. Even in nations where malaria is common, when a solid diagnosis based on microscopy and rapid diagnostic testing is becoming the norm, it is becoming increasingly clear that most cases of fever have other causes (*i.e.*, nonmalarial febrile illness). In regions where malaria has been effectively controlled through various methods, the issue is particularly evident. The patient's malaria test came back negative, but their symptoms persisted. **Figure 1** shows the major causes of acute febrile diseases, highlighting the need for comprehensive diagnostic approaches. Acute febrile syndrome is a group of symptoms that may appear suddenly and have several probable causes, one of which is malaria [14]. Malaria is only one of many disorders that, despite their potentially fatal symptoms, can be cured with rapid diagnosis and treatment [15].

A complete strategy for treating acute febrile syndrome must include the latest knowledge on the prevalence of numerous causes of febrile disease, creating innovative diagnostic and therapeutic instruments, and building long-term treatment algorithms and supporting infrastructure (AFS). There are possibilities and difficulties in addressing these concerns, which have far-reaching effects throughout the healthcare system.

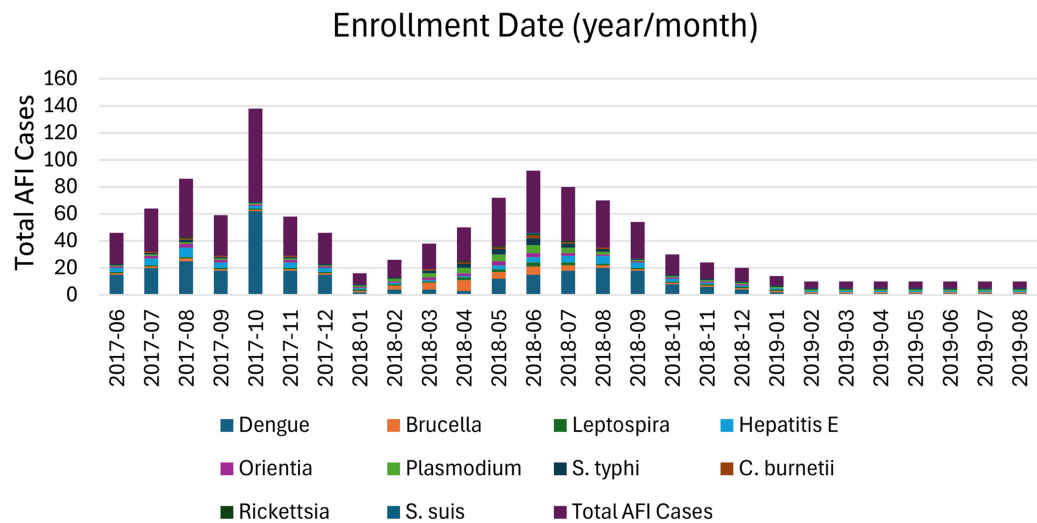


Figure 1. Major causes of acute febrile disease (Adapted from Grundy [16]).

Using state-of-the-art diagnostics will improve the prospects for disease control and eradication in low-resource countries in the future. Community progress toward economic independence can be slowed by the possibility of economic consequences caused by fever [15]. Due to factors such as the price of medical care, the loss of a family breadwinner due to illness, a drop in income due to time off work, and the emotional toll of a family member's death, the financial and human costs of severe illness and the high transmission of infectious disease are difficult to evaluate. The worst effects of climate change are controllable and curable, but people must have access to the resources they need to reduce their severity. By combining demands to enhance malaria diagnosis with the need to address alternative causes of fever and what to do when the malaria test result is negative, FIND HOPES concentrates on developing tools for diagnosing acute fever. Malaria diagnosis is the subject of separate research, whereas here, we will examine an AFS-unrelated strategy [17].

4. Improving Diagnosis of NMFI

When a patient in an endemic area presents with a fever, the first step in therapy is to perform a microscope or RDT test for malaria. Test results are typically negative since there are many other possible explanations for a high body temperature besides malaria. A difficult situation arises when a healthcare professional is faced with a patient still seeking treatment but with limited diagnostic tools at his disposal. Without medical intervention, the patient's condition may improve to the point of full recovery or worsen to the point of death. Nonmalarial febrile infections cause the most deaths worldwide, although they are often treatable if caught and treated early enough [2]. In most cases, optimal therapy for nonmalarial fever can be achieved without knowing the condition's exact cause.

Certain causes of fever are quite modest and self-limiting, needing only temperature management or attentive observation, and these are universal in cultures

and societies. The illness will clear up in a day or two. Such is frequently observed in illnesses primarily affecting the throat, notably those of viral origin [18]. The World Health Organization issued guidelines for the integrated treatment of childhood illnesses (IMCI) and illness in teens and adults (IMAI) to help doctors. Clinical diagnosis, made through in-depth questions, careful observation, and a thorough physical examination, can sometimes help guide treatment. However, an accurate clinical diagnosis is hard and not very specific. As a result, it cannot distinguish between many potentially serious infections in the early stages when treatment is most effective. For example, bacterial meningitis remains a problem in developing countries but is rare in regions with robust health systems and accurate early diagnosis. Diagnostic tests give doctors the information they need to make an early, effective treatment plan. They do this by finding signs that a single patient needs special care or providing information about how common a disease is to support a clinical diagnosis [19].

5. Acute Febrile Syndrome (AFS) in Low-Resource Settings

In low-resource countries, community point-of-care diagnostics are not good enough, even though early sickness management is most effective at this level. However, many current solutions are either too costly, too technically sophisticated or require too many resources in the laboratory to be practical in real-world settings [3]. Some of the leading causes of death and serious illness in tropical and subtropical climates are not recognizable even at the hospital level.

However, in low-resource, high-burden countries, various cutting-edge or well-established technologies are already used to treat acute infectious febrile diseases. Examples are microscopes and lateral flow rapid diagnostic tests (RDTs) for diagnosing diseases including malaria, HIV, syphilis, and others. To address these diseases, alternative, more modern technologies are already in place in countries with a high standard of living. Near-field applications of nucleic acid detection tests (NAATs) are being developed and improved, with tests such as LAMP assays for malaria and trypanosomiasis (the cause of sleeping sickness) and GeneXpert for detecting TB becoming increasingly accurate and usable. In low-resource countries, there is a lack of diagnostic tools for the causes of AF despite the huge potential for a paradigm shift in the treatment of acute fever and the reduction of avoidable morbidity and mortality. Investment in new and existing technology that can meet the needs of high-burden illnesses in these settings is essential to reduce poverty and the large societal costs of widespread disease [20].

6. Treatment Strategies for AFS

Existing and prospective technologies (malaria and nonmalarial febrile disease)

- Microscopy using visible light.
- Rapid diagnostic tests (RDTs) are lateral-flow (immune chromatic-graphic) assays.

- Aptamers for Detecting Nucleic Acid Amplification (NAAT).
- Quantitative enzyme immunoassay (ELISA).
- Advanced, ever-evolving technology [16].

It is readily available, has shown usefulness in disease management, and may be used to identify and quantify various organisms based on their morphology. It is inexpensive, flexible, and perhaps locally sponsored. The dependability of the results varies widely depending on the skill level of the user and the quality of the reagents used, which is a major drawback. The number of microorganisms in a sample, proper collection, and staining all contribute to an assay's sensitivity and are widely useful in clinical settings, but they are not applicable to many conditions or are not feasible at the village level. RDTs can be inexpensive compared to microscopy and require less training and support [21].

The prevalence of some diseases, such as malaria, syphilis, and HIV, is well documented. They are limited in their ability to detect various illnesses since they can only identify particular organisms, and it is difficult to integrate tests for several diseases into a single test. Nucleic acid (DNA or RNA) detection assays are often used as gold standards due to their high sensitivity [6]. Polymerase chain reaction (PCR) tests are the most common type, but they are costly and time-consuming to run in the lab, making them impractical for use in emergencies. Low-cost near-patient testing is possible with the help of new technologies that streamline heating procedures, sample preparation, and interpretation of data for use in resource-limited areas. As a result, the precision of point-of-care tests, such as loop-mediated isothermal amplification (LAMP), can be dramatically improved. Nevertheless, not many can be used to diagnose nonmalarial fever. Established procedures are particularly used in screening and reference laboratories.

Due to the need for specialized training and equipment, case management is unsuitable for low-resource inpatient settings. Several types of cutting-edge tools are now in development, including ones based on photonics, ones that detect chemical markers uniquely, and others that modify traditional tools with cutting-edge tech (such as digital microscopy) [10]. Resource-rich regions may already possess access to some of these advanced diagnostic tools. As low-resource settings cannot now accommodate the target illnesses or the maintenance expenses of existing applications, the latter are severely constrained. However, such innovations will eventually be required to identify the variety of infections needed to guide efficient treatment of fever at the cost and simplicity required to ensure easy access to people in need. That is why it is important to have a holistic strategy considering both short- and long-term objectives [22].

7. Diagnostic Methods for Acute Febrile Illness

Why accurate data are essential for efficient disease management?

- Effective fever treatment necessitates identifying the underlying cause, which is crucial for healthcare providers and patients [22].
- To best use their limited resources, healthcare providers must know how often

fever-causing conditions occur and where they happen [23].

- To maximize the positive effect of the funds they allocate on public health, funding organizations require these data to make funding decisions.

The diagnosis is meant to provide this information, separating the causes of acute febrile syndrome into their component disorders so that appropriate care can be administered, such as treating a sick individual with acute fever in a malaria-endemic region as a person who may have [24].

- Malaria: Treatable; must be detected quickly.
- Severe NMFI: Various illnesses that can become fatal; mostly treatable; must be detected quickly [25].
- Mild NMFI: Minor infections clear up on their own, such as a viral respiratory tract infection; supportive treatment; patient can be safely sent home [11].

8. A Public Health Approach to AFI

In a setting with limited resources, the focus should be on delivering critical data that can directly or indirectly influence patient care using sustainable methods. A 3-stage progression model can be used to summarize these key points:

- Understanding the root causes of the disease is the first step in improving current clinical algorithms [5].
- Develop diagnostic measures of therapeutic efficacy and severity (MSR).
- Finally, tests for specific, treatable infections that are likely to be found should be designed and implemented, ideally in a multiplex format (e.g., with malaria tests) [21]. **Figure 2** displays the etiology of acute febrile illness.

Organizations seek the input of modelers and health economists throughout this development process to determine which diagnostic intervention tactics and investments yield the highest return on investment. Enhancing diagnostic specificity and precision necessitates increased investment in patient treatment, product development, and subsequent distribution [19]. However, the social and economic benefits of better health are much greater. Careful consideration of these aspects is required from healthcare service providers, product developers, and sponsors. A syndrome is called a group of symptoms (such as fever, a headache, and others) that appear suddenly and might have several causes. A pathological abnormality or set of abnormalities causes a disease, defined as a change in the normal structure and/or function of the body. Both malaria and nonmalarial diseases, such as typhus, typhoid, and pneumonia, cause acute febrile syndrome. Care that addresses the root cause and provides health services with the information they need to set priorities and make plans requires a high degree of differentiation between them.

The consequences of this may include [1]:

- Case management verification procedures (tests to guide treatment where patients first seek care).
- Prognostic tests are used to find the most common pathogens in a group of people so that they can be treated and planned [7].

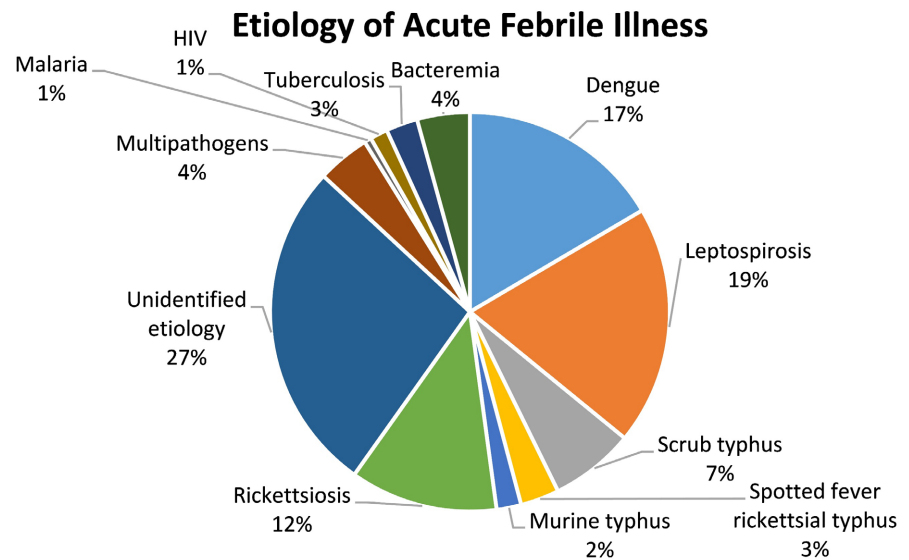


Figure 2. Etiology of acute febrile illness (Adapted from Shimelis, [13]).

9. Advancing Point-of-Care Diagnostics

Given the limited resources and workforce available in low-income nations, diagnostic therapies with the highest potential for beneficial effects must be prioritized.

- Boost the performance of currently used medicines [26].
- Make sure that diagnostics and treatment plans are tailored to the skills and resources of physicians and other healthcare professionals. As a result, the need for additional logistics and other resources for health services will be reduced [25].
- Whenever possible, national health programs should prioritize tests and platforms that are backward compatible with already-existing technology to lessen their need for costly long-term external maintenance (such as malaria testing) [23].

10. Current and Future Projects

From now on, businesses will focus on a small number of areas that, if done right, will lead to measurable results. The goal of the approach is to make it easier for community healthcare providers and implementers to create tools they can use. Such collaborative efforts will be facilitated by specialist partners contributing their expertise and knowledge [27]. **Table 1** below outlines the strategic framework for developing diagnostic tools for nonmalarial febrile illnesses (NMFIs).

Table 1. Strategic framework for developing diagnostic tools for Nonmalarial Febrile Illnesses (NMFIs).

Tier	Goal	Activities
Tier 1: Population screening and mapping	Understand the prevalence and distribution of NMFIs.	<ul style="list-style-type: none"> - Develop an interactive database to track and map pathogen presence. - Adapt existing laboratory-based multiplex screening technologies for large-scale population screening.

Continued

Tier 2: Tests for Markers of Severity and Responsiveness (MSR) to treatment	Identify individuals at risk of severe illness and predict treatment response.	<ul style="list-style-type: none"> - Identify non-specific indicators of disease severity. - Conduct field trials of point-of-care (POC) lateral flow tests for MSR. - Evaluate existing pathogen-specific assays. - Assess the feasibility of multiplex platforms for POC diagnostics. - Develop and adapt POC platforms targeting high-burden and treatable pathogens.
Tier 3: Pathogen-specific tests	Develop accurate and rapid tests for specific NMFI-causing pathogens.	<ul style="list-style-type: none"> - Evaluate existing pathogen-specific assays. - Assess the feasibility of multiplex platforms for POC diagnostics. - Develop and adapt POC platforms targeting high-burden and treatable pathogens.
Enabling methods and technologies	Supporting activities.	<ul style="list-style-type: none"> - Develop simplified instructions and training materials. - Improve blood/specimen transfer devices. - Utilize electronic/SMS-based systems for commodity tracking and results management. - Standardize methods and devices for integration with other disease management programs. - Develop tests to detect markers of microbial resistance. - Develop companion diagnostics to confirm drug safety and guide dosing.
Impact modelling and cost-benefit analysis	Ensure effective resource use and maximize public health impact.	- Conduct impact modeling and cost-benefit analyses throughout the process.

11. High-Throughput Screening and Mapping

Diseases may differ in prevalence from one area to another. An example of a clinical algorithm with wide applicability is the World Health Organization (WHO) protocol for the Integrated Management of Childhood Illness (IMCI). It is assumed that the global prevalence of different fever causes is roughly the same, so we apply a standard clinical approach everywhere. Without additional data on the prevalence and distribution of diseases worldwide, we cannot tailor universal methods such as IMCI to local conditions and ensure precise drug targeting and prompt and efficient treatment [26].

Pathogen prevalence has been studied on a smaller scale in some countries. However, conventional reference methods such as polymerase chain reaction (PCR) and blood culture are time-consuming, labor-intensive, and costly, and they need to be periodically repeated because prevalence can change with economic and environmental factors. Careful extraction and mapping of the existing literature can reveal a wealth of information on the prevalence of infections gathered accidentally through researching various diseases.

As a result of technological advancements, it is now possible to conduct comprehensive surveys of various diseases at a cost much lower than that of conventional laboratory analysis. If these methods were perfected and used, we would better understand where and how widespread nonmalarial infections are. The clinical algorithms might then be fine-tuned for more targeted treatment afterward. Data like this provide both facts and a theoretical framework that may be

used to prioritize diagnostic development [27].

12. Markers of Severity and Responsiveness (MSR)

The findings may go beyond what can be learned from a simple clinical exam if he or she can notice signs of how bad a disease is or how sensitive a patient is to certain drugs. A clinic or health center in a remote area may use this metric to decide whether to send a patient home after a brief stay or to send them for further testing and treatment [6]. Such information could determine whether a patient requires costly hospital treatment. Pathogens that are “one-of-a-group” of pathogens susceptible to a certain antimicrobial can be used as markers to guide targeted and effective therapy without finding the real cause of the illness. Fortunately, tetracyclines and other antibiotics can treat infections caused by rickettsia.

Differential white blood cell counts, blood glucose concentration, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), procalcitonin, and ESR are all examples of markers now used. Information on the community-level specificity of these markers is rare in tropical and subtropical regions. Understanding the specificity of markers, identifying new markers, and incorporating these into single or multiplex point-of-care tests can greatly advance patient care [11].

13. Infections Causing AFI by Location

In addition to malaria, other nonmalarial diseases that may be tested right at the point of care (POC) include typhus, typhoid, and dengue. Several diagnostic instruments are either too expensive or general to be useful in low-income areas (poorly sensitive). The value of these POC tests for sick people depends on how easy they are to get, how much they cost, and how they affect the treatment options that doctors and nurses can use [7].

The most common infections that cause fever, and the best tests to determine what is wrong will differ depending on location. Visually interpreted lateral flow tests, which are often used for testing in the community, do not have much potential for multiplex testing, which is when a single test can find electronic readers that may be more flexible, but they cost more and require more advanced equipment. Many other diagnostic systems are in the works, but none are economical or practical enough to be used in a rural clinic or community. More studies and development of these tests will help diagnose diseases that cause fevers [28].

14. Modeling and Cost-Benefit Analysis

Limited resources in under-resourced regions hinder the utilization of diagnostic tests due to financial constraints on research, development, and available materials. As diagnostic accuracy increases for specific diseases, so do the associated testing costs. The success of these studies relies on cost-effectiveness for both sponsoring organizations and low-income participants. Effective research and development prioritization necessitates expertise in disease management, predictive modeling, and comprehensive cost-benefit analysis. To identify attainable goals,

focused partnerships concentrating on product development and organization should seek guidance from diverse groups [20].

15. Effective Regional Rollout of Diagnostics

Diagnostic interventions are more likely to be used if diagnostic tests are useful, if health professionals know how to use diagnostic tests well, and if the system for getting high-quality diagnostics and the needed treatment works well. A good procurement policy, adequate training and supervision, an organized supply chain, and a focus on reducing waste are all needed.

When bringing this to a remote location, it can be difficult for healthcare providers and product developers because they need to provide tests that can be used with a wide range of platforms. Although the organization is not primarily a health system support group, we recognize the potential benefits of cutting-edge technology that can be used in the real world. Without this, disease prevention programs might take a long time to adopt new technology [22]. Companies will continue working closely with health authorities and implementation groups to address critical areas of need, such as hurdles to general adoption that apply to our product line, and optimize the return on investment for diagnostic R&D efforts [29].

15.1. Aid in The Diagnosis of Drug Problems

Due to how common and changeable drug resistance is in treating a wide range of infectious agents, it is important to watch for it and find ways to determine how susceptible a person is to pathogens. Some people may be more likely to be sick from the side effects of certain drugs because they already have or were born with a problem with how they respond to medications. When the bacteria that cause NMFI are better controlled, these diagnostics will likely be important for controlling several disorders. To get the most from pharmacological benefits, patient care must be safe and effective, and needs must be met as soon as they become clear [18].

15.2. More Funding for the Diagnosis of Acute Fever Sickness Is Reasonable

Most of the money and help goes to programs that help people get vaccinated and avoid HIV/AIDS, TB, and malaria. Even when there is a clear overlap between these priority diseases, funding organizations may not have the political and structural flexibility to treat other causes of fever. It was difficult to treat non-TB respiratory disorders with any of these three treatment plans [15].

There is no major monetary “champion” in diagnostics for nonmalarial febrile illness; hence, progress in this area has been slow. Having up-to-date information on how often diseases occur is important for fine-tuning the focus of different treatments to make them work better. The evident public health benefits of reduced convalescence periods and decreased disease transmission and mortality

risks complement these advantages. Investing in diagnosis can have far-reaching effects that go beyond direct treatment. For example, it can increase the value of money spent on other types of health care and lower the costs of implementing them. When it comes to infectious diseases in low-resource countries, HIV, malaria, and tuberculosis receive the vast majority of funding for research and development. Less money has been spent researching and developing treatments for the other possible causes of sudden high fever. On the other hand, diagnostics R&D only receives 3.2% of total R&D funding. Budgets for diagnostics research and development are limited, and most other causes of acute fever beyond malaria are not even considered. **Table 2** below displays the proportional spending on research and development for infectious diseases in low-resource settings in 2009.

When it comes to infectious diseases in low-resource countries, HIV, malaria, and tuberculosis receive the vast majority of funding for research and development. Less money has been spent researching and developing treatments for the other possible causes of sudden high fever. On the other hand, diagnostics R&D only receives 3.2% of total R&D funding. Budgets for diagnostics research and development are limited, and most other causes of acute fever beyond malaria are not even considered [26].

The potential alteration of the epidemiology of acute febrile diseases requires a long-term investment in novel diagnostics. Although increasing spending on research in many important areas of healthcare in low-resource settings will have a large effect, increasing diagnostics from a very low base could lead to lower mortality and better public health in a relatively short time. Integrating complementary and alternative medicine into conventional medical practices is possible. In the next few years, much can be done with smart spending [30].

Table 2. Proportional spending on research and development for infectious diseases of low-resource settings in 2009.

Research & development area	Spending (%)
Vaccines	54.4
Basic research	32.5
Drugs	5.1
Unspecified	3.7
Diagnostics	3.2
Vector control	1.1

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- A world map showing the prevalence of the most common nonmalarial causes of fever so that gaps in knowledge can be filled with more research [9].
- A high-throughput screening method has been found and shown to work, making it possible to estimate the number of pathogens in the future.
- Determination of the clinical utility of currently available candidate severity

and treatment response indicators (MSR) and the feasibility of their implementation into disease-specific point of care (POC) testing [20].

- A proven, fully integrated, and scalable national-level e-information system for managing commodities, reporting diseases, and directing patients to long-term care in at least one country.
- The potential of several multiplex platforms has been tested in the field.
- At this time, at least one major field study is being conducted [31].
- For use in places with few resources and that are not easy to access, it is important to standardize instruction forms and blood transfer across commonly used point-of-care assays. Novel point-of-care (POC) diagnostics for high-burden diseases: a feasibility analysis [25].

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- Extensive information on the prevalence and distribution of major pathogens, including in all densely populated tropical and subtropical regions, was gleaned from high-throughput screening surveys [30].
- In many areas, lateral flow malaria tests have been replaced with multiplex point of care (POC) assays that identify the disease and have at least MSR detection capabilities.
- In other areas, treating nonmalarial febrile diseases has been integrated with malaria control and elimination [7].
- A significant reduction in mortality from fever, especially in children, is achieved through routine use of early case management [6].
- At least three to four main high-burden pathogen-specific tests are routinely used in high-prevalence areas (common lower respiratory tract infections, typhus, typhoid).
- Multiple examples of fully integrated multiplex tests at the hospital/outpatient triage level led to lower admission rates, earlier discharge, and lower inpatient mortality [16].

With enough money and a well-coordinated, logical plan, the way acute febrile illness is treated in low-income communities, where death for no reason is still common, could be greatly improved in the future. Such an impact could significantly improve public health and community quality of life [31].

16. Conclusions

Nonmalarial febrile illnesses (NMFIs) pose a significant health concern in low-income countries, particularly affecting children. These illnesses, caused by various diseases, can be effectively addressed with minimal resources through preventative measures. Developing simple, low-cost, and accurate diagnostic tools to identify specific diseases and predict severe outcomes could greatly enhance public health. The healthcare sector now has advanced tools for outcome management and supply chain sustainability, which can revolutionize health systems management, disease surveillance, and illness control.

As malaria prevalence declines in many regions, healthcare systems must pri-

oritize identifying and treating secondary causes of fever. The urgent need for increased investment in research and development of diagnostic tools for NMFI is underscored, as this could significantly reduce mortality rates and improve public health outcomes. Strategic investment in this area can bring substantial improvements in the coming years.

Creating a global map of the most common causes of nonmalarial fever could highlight areas that need further research. Other potential advancements include developing high-throughput screening methods to predict future pathogen numbers, determining the clinical usefulness of existing severity and treatment response indicators, and establishing a robust national e-information system for managing commodities, reporting diseases, and directing patients to long-term care. High-throughput screening surveys will likely provide extensive information on major pathogens' prevalence and distribution. Multiplex point-of-care assays with MSR detection capabilities are expected to replace lateral flow malaria tests in many regions.

With adequate funding and a coordinated, strategic approach, significant advancements can be made in addressing acute febrile illnesses in low-income communities, leading to substantial improvements in public health and quality of life.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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