IntechOpen

Neglected Tropical Diseases
Unsolved Debts for the One Health Approach

Edited by Jorge Abelardo Falcón-Lezama and Roberto Tapia-Conyer

Neglected Tropical Diseases - Unsolved Debts for the One Health Approach

Edited by Jorge Abelardo Falcón-Lezama and Roberto Tapia-Conyer

Published in London, United Kingdom

Neglected Tropical Diseases - Unsolved Debts for the One Health Approach
http://dx.doi.org/10.5772/intechopen.1000395
Edited by Jorge Abelardo Falcón-Lezama and Roberto Tapia-Conyer

Contributors
Jorge Abelardo Falcón-Lezama, Roberto Tapia-Conyer, Talabi Helen Bamikole, Diego-Abelardo Álvarez-Hernández, Daniella Pinto, Luis Martínez-Juárez, Rodolfo García-Rodríguez-Arana, Alejandra Montoya, Nádia Teresinha Schröder, Eliane Fraga Da Silveira, Letícia Thomasi Janhke Botton, Eduardo Périco, Kingford Chimfwembe, Christopher Simoonga, Hikabasa Halwindi, Rockiner Simoonga

First published in London, United Kingdom, 2024 by IntechOpen
IntechOpen is the global imprint of INTECHOPEN LIMITED, registered in England and Wales, registration number: 11086078, 5 Princes Gate Court, London, SW7 2QJ, United Kingdom

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

Additional hard and PDF copies can be obtained from orders@intechopen.com

Neglected Tropical Diseases - Unsolved Debts for the One Health Approach
Edited by Jorge Abelardo Falcón-Lezama and Roberto Tapia-Conyer
p. cm.
Print ISBN 978-0-85466-068-1
Online ISBN 978-0-85466-067-4
eBook (PDF) ISBN 978-0-85466-069-8

Meet the editors

Dr. Jorge Abelardo Falcón-Lezama obtained his medical degree from the Juárez Autonomous University of Tabasco, a master's degree in infectious diseases from Mexico's National Institute of Public Health, a Ph.D. in Epidemiology from the National Autonomous University of Mexico, and a specialization in intelligence for national security from Mexico's National Institute of Public Administration. Dr. Falcón-Lezama has worked at Morelos State Health Services, Mexico's Institute for Insurance and Social Services for the State Workers, Juarez Autonomous University of Tabasco, and the Carlos Slim Foundation. He has taught postgraduate courses at the National Polytechnic Institute, Juarez Autonomous University of Tabasco, and Hidalgo State Autonomous University. As a researcher, his interest is focused on the epidemiology, surveillance, and prevention of infectious diseases as well as emerging and neglected tropical diseases. He is the author and co-author of more than twenty scientific manuscripts and book chapters, editor of two books, and invited academic editor and reviewer of several scientific journals. He is a member of Mexico's National System of Researchers and the Mexican Public Health Association.

Dr. Roberto Tapia-Conyer obtained an MD from the National University of Mexico (UNAM). He also holds master's degrees in science and public health from Harvard University, USA, and a doctorate in sciences from UNAM. His career has transcended the common limits of the health expert, combining his medical vision with innovation, creativity, technological development, and a marked emphasis on human and gender rights. Innovation with a social perspective is the common denominator of his career. Dr. Tapia-Conyer is a member of the National System of Researchers of the National Council of Humanities, Sciences and Technologies (CONAHCYT) Level III. He is also a member of the National Academy of Medicine of Mexico, the National Academy of Surgery, the Mexican Academy of Sciences, and the Mexican Society of Public Health. For 25 years, Dr. Tapia-Conyer dedicated himself to public service in the Federal Ministry of Health, where he held positions from which he led the generation of public policies, the foundation of current health programs on issues such as addictions, vaccination, and HIV and AIDS. He also established the current National Epidemiological Surveillance System and the National Health Survey System. For 45 years he has worked as a professor at the UNAM Faculty of Medicine, an institution that awarded him the medal for University Merit and that successfully nominated him to receive the 2017 Medical Merit Award, the most important recognition in the field in Mexico. In addition, he has been a visiting professor at the University of California, at the San Francisco, Berkeley, and Irvine campuses. He currently serves as General Director of the Carlos Slim Foundation, from where he has created and promoted a broad agenda of innovations in digital health, in addition to coining the concept of Personalized Public Health.

Contents

Preface

Why is it still important to write about neglected tropical diseases (NTDs)? There are many answers to this simple question. The most obvious is that at the dawn of the 21st century, there is still a debt owed to the more than one billion people at risk of becoming ill with NTDs.

The timing seems strange as it is just after the world rejoices at having brought COVID-19, the most significant event in public health in the last 100 years, somewhat under control. Nonetheless, we think that today, when most health systems are already planning their response to the next pandemic, is the best time for our contribution, taking advantage of the inertia that the world brings about the importance of public health and with the certainty that, when applied appropriately, disease prevention and control measures work and achieve their objectives for the benefit of populations.

This book represents our small contribution to the effort to provide health professionals with the tools to face the challenge that NTDs represent, especially in the most affected geographic regions. As editors, but mainly as public health specialists, we think that as long as neglected tropical diseases exist, this topic is one that cannot be written about excessively. However, even more importantly, it cannot be allowed to be put aside on the list of global health priorities.

The book includes five chapters. Chapter 1 briefly explores the general causes of NTDs, provides insight into their status, and reviews the challenges inherent in their control. Chapters 2 and 3 review two of the most emblematic diseases within this group of diseases: malaria in Africa and Chagas disease in Latin America. Both diseases represent formidable challenges for health systems struggling to provide alternatives and solutions to the populations under their care. Finally, Chapters 4 and 5 highlight some of the tools that health systems have at their disposal to address these diseases.

Finally, we thank the millions of health workers who do their part every day in the fight against these diseases. We are also grateful to our collaborators who kindly sent us their contributions and patiently worked with us to compose this book. Without their immeasurable support, the publication of this volume would not have been possible.

Jorge Abelardo Falcón-Lezama
Health Sciences Academic Division,
Juarez Autonomous University of Tabasco,
Villahermosa, Tabasco, México

Roberto Tapia-Conyer
Faculty of Medicine,
National Autonomous University of Mexico,
Mexico City, México

Chapter 1

Introductory Chapter: Neglected Tropical Diseases – A Pending Issue

Jorge Abelardo Falcón-Lezama and Roberto Tapia-Conyer

1. Introduction

Defined as the study of complex change in patterns of health and disease and on the interactions between these patterns and their demographic, economic and sociologic determinants, and consequences [1], epidemiologic transition has changed population health in the last century. This global phenomenon is characterized by two major components: (1) changes in population's age distribution from younger to older and (2) changes in patterns of morbidity and mortality [2], being the shifting from infectious to noncommunicable diseases as the leading causes of mortality and disease burden, its most evident effect. As a result, new challenges arise, and priorities must be reshuffled to provide quality and effective health interventions.

Despite of today's spectacular advances in public health, benefits have not reached all geographic regions at the same pace, creating mixed scenarios in which a double disease burden, one from new challenges typical from developing countries arise and other in which old unsolved problems remain [3]. These pockets of lagging conditions are ideal for the persistence of a group of diseases that remain major unsolved health problems. Those are the neglected tropical diseases (NTDs).

2. Neglected tropical diseases today

Neglected tropical diseases (NTDs) are a diverse group of diseases that occur in tropical and sub-tropical regions and are intimately linked to poverty and other social conditions [4]. Globally, one out of six inhabitants are at risk [5]; nonetheless, this frequency is not homogeneously distributed but focused instead on specific geographic regions such as sub-Saharan Africa, Asia, and Latin America.

The most recent list of NTDs includes Buruli ulcer, Chagas disease, dengue and chikungunya, dracunculiasis, echinococcosis, foodborne trematodiases, human African trypanosomiasis, leishmaniasis, leprosy, lymphatic filariasis, mycetoma, chromoblastomycosis and other deep mycoses, onchocerciasis, rabies, scabies and other ectoparasitoses, schistosomiasis, soil-transmitted helminthiases, snakebite envenoming, taeniasis and cysticercosis, trachoma, and yaws [6].

As for their impact in population's health, NTDs not only account for mortality or morbidity but also are a cause of disabilities and other effects such as the impairment of the cognitive development of children which ultimately affect permanently the quality of life in those affected individuals. Finally, while considering both direct and indirect costs, they can easily be catastrophic for individuals and families.

3. The challenge and new tools for addressing neglected tropical diseases

Neglected tropical diseases (NTDs) are difficult to address due to multiple factors. As for their nature, they are a diverse group of bacterial, viral, fungal, and noncommunicable diseases with environmental components in their natural history that make difficult the design of stand-alone interventions. Very few of them have specific vaccines, or treatments that are widely available or easily deployable, and most require follow-up of the cases to achieve complete recovery.

Ideally, multiple and coordinated interventions are required over time to achieve the desired impact. Most interventions can be classified into three types: (1) preventive chemotherapy by mass drug administration, (2) innovative and intensified disease management, and (3) vector ecology and management. Many NTDs require all three types of interventions in a comprehensive approach for extended periods. This is expensive, as it represents the overall cost of billions of dollars every year; nonetheless, this approach has proven to be cost-effective [7].

Today, no country by itself can address NTDs as an isolated entity, as it requires sufficient resources and investments that not all countries can afford. Most of the research infrastructure and networks are not located in affected regions, and the countries with access to them (usually developed countries) not necessarily have NTDs at the top of their priorities; therefore, multilateralism and cooperation are also required.

Finally, understanding the social context is essential while addressing NTDs. Factors such as high poverty rate, large immigrant population, geographic proximity to endemic areas [8], and social unrest are common in many of the regions where NTDs are highly prevalent and need to be taken into consideration while planning and implementing interventions.

The World Health Organization endorsed by the 73rd World Health Assembly, the initiative Ending the neglect to attain the Sustainable Development Goals. Roadmap for neglected tropical diseases 2021–2030 [6], thus setting the starting point to a new priority in which all State members define their specific plans to address NTDs in the coming years.

In the meantime, science is one of the best allies for tackling NTDs. Once an NTD, malaria, is still today the main killer in the world. Until 2021, Malaria vaccine had been an elusive dream [9], but only 2 years later, the mass allocation of doses for the most affected countries in Africa is a reality that will deliver positive impacts in the coming years [10]. This step has taken over 40 years of research and considerable investment but has marked the trajectory that needs to be followed if we want to succeed in this pending issue.

4. Conclusions

Epidemiologic transition is a reality and a process that will continue to develop as societies evolve. The main task health systems will face in the future is to manage this transition in an orderly fashion for avoiding gaps and inequities that facilitate NTDs and simultaneously providing benefits to most of the population. This is no minor task as it requires planification, coordination, and most importantly long-term and persistent commitment, one that has been present only on a few occasions in public health history. More than a pending issue, NTDs existence in the 21st century is a general failure of our societies which needs to be properly addressed and solved.

DOI: http://dx.doi.org/10.5772/intechopen.1004351

Author details

Jorge Abelardo Falcón-Lezama[1*] and Roberto Tapia-Conyer[2]

1 Health Sciences Academic Division, Juarez Autonomous University of Tabasco, Villahermosa, Tabasco, Mexico

2 Faculty of Medicine, National Autonomous University of Mexico, Mexico City, Mexico

*Address all correspondence to: jorgefalcon@hotmail.com

IntechOpen

References

[1] Omran AR. The epidemiologic transition. The Milbank Memorial Fund Quarterly. 1971;**49**:509-538

[2] McKeown RE. The epidemiologic transition: Changing patterns of mortality and population dynamics. American Journal of Lifestyle Medicine. 2009;**3**(1 Suppl):19S-26S. DOI: 10.1177/1559827609335350

[3] Adogu POU, Ubajaka CF, Emelumadu OF, Alutu COC. Epidemiologic transition of diseases and health-related events in developing countries: A review. American Journal of Medicine and Medical Sciences. 2015;**5**(4):150-157. DOI: 10.5923/j.ajmms.20150504.02

[4] WHO. Working to Overcome the Global Impact of Neglected Tropical Diseases. First WHO Report on Neglected Tropical Diseases. Geneva: Word Health Organization; 2010. Available from: https://www.who.int/neglected_diseases/resources/9789241564090/en/ [Accessed: December 14, 2019]

[5] Mathers CD, Ezzati M, Lopez AD. Measuring the burden of neglected tropical diseases: The global burden of disease framework. PLoS Neglected Tropical Diseases. 2007;**1**(2):e114. DOI: 10.1371/journal.pntd.0000114

[6] World Health Organization. Ending the Neglect to Attain the Sustainable Development Goals: A Road Map for Neglected Tropical Diseases 2021-2030. Geneva: World Health Organization; 2020. [Licence: CC BY-NCSA 3.0 IGO]

[7] Fitzpatrick C, Nwankwo U, Lenk E, de Vlas SJ, Bundy DAP. An investment case for ending neglected tropical diseases. In: Holmes KK, Bertozzi S, Bloom BR, et al., editors. Major Infectious Diseases. Washington (DC): The International Bank for Reconstruction and Development/The World Bank; 2017

[8] Hotez PJ, Bottazzi ME, Dumonteil E, Valenzuela JG, Kamhawi S, Ortega J, et al. Texas and Mexico: Sharing a legacy of poverty and neglected tropical diseases. PLoS Neglected Tropical Diseases. 2012;**6**(3):e1497. DOI: 10.1371/journal.pntd.0001497

[9] Zavala F. RTS, S: The first malaria vaccine. The Journal of Clinical Investigation. 2022;**132**(1):e156588. DOI: 10.1172/JCI156588

[10] World Health Organization 18 Million Doses of First-Ever Malaria Vaccine Allocated to 12 African Countries for 2023-2025: Gavi, WHO and UNICEF [Internet]. 2023. Available from: https://www.who.int/news/item/05-07-2023-18-million-doses-of-first-ever-malaria-vaccine-allocated-to-12-african-countries-for-2023-2025--gavi--who-and-unicef

Chapter 2

Confronting Malaria – Addressing a Critical Health Crisis among Vulnerable Groups in Nigeria

Talabi Helen Bamikole

Abstract

Malaria is caused by parasites of the Plasmodium genus and transmitted to humans through infected Another's bites. The common symptoms are fever, headaches and chills. The parasites enters the blood stream and infect the red blood cells. Malaria can be treated with anti-malarial drugs and it can also prevented using mosquitoes bed net and repellant.

Keywords: malaria, children, pregnant women, age, bite, plasmodium, Nigeria

1. Introduction

Malaria is an important neglected tropical disease (NTD) that has a substantial impact on a large population across the globe, with a particular focus on tropical and subtropical areas. The etiology of this condition can be attributed to a specific microorganism belonging to the genus Plasmodium, which is classified as a protist. Malaria fever is the result of being bitten by mosquitoes carrying the malaria parasite. The transmission of the disease occurs solely through the bites of *Anopheles* mosquitoes that are infected.

The symptoms may range from mild to severe, potentially posing a threat to one's life. Common symptoms include a low-grade fever, accompanied by chills and a headache. Prominent manifestations encompass profound fatigue, cognitive impairment, epileptic episodes, and respiratory distress.

Malaria presents a significant global health challenge, particularly in nations with limited economic resources. Based on data provided by the World Health Organization (WHO), it is estimated that there were approximately 241 million instances of malaria and 627,000 fatalities in the year 2020, with the majority of cases concentrated in the sub-Saharan African region. The disease exhibits a disproportionate impact on populations that are particularly vulnerable, such as young children and pregnant women, thereby leading to elevated rates of morbidity and mortality [1].

Malaria prevention can be achieved through the implementation of strategies aimed at minimizing mosquito bites and the utilization of appropriate pharmaceutical interventions. The implementation of treatments has the potential to prevent the progression of mild cases.

Anopheles mosquito bites from females that have been infected with malaria are the main way that the disease is spread. Additionally, blood transfusions and the use of contaminated needles are two ways that malaria can be spread. The initial symptoms of malaria can often be mild, resembling various febrile illnesses, which can make it challenging to promptly identify the disease. If left untreated, *P. falciparum* malaria has the potential to rapidly advance into a severe medical condition, ultimately resulting in mortality within a span of 24 hours.

1.1 Ecology of the vector

The presence of malaria vectors can be influenced by climatic conditions. For example, Ojo and Mafiana [2] noted that the equatorial region provides favorable conditions for mosquito growth, while the low incidence of malaria in Northern Africa may be attributed to the dry Sahara Desert. The transmission of malaria depends on the presence of human hosts carrying Plasmodium parasites and a sufficient number of anopheline mosquitoes in suitable environmental conditions, particularly temperature and humidity [3].

The morbidity and mortality rates associated with malaria are influenced by various factors [2]. According to Nasir et al. [4], *Plasmodium* undergoes complex development and multiplication processes in both humans and mosquitoes before it can be transmitted further. Thus, understanding the ecology of these vectors is crucial for malaria eradication efforts. Mosquito ecology is closely linked to poor sanitation, as unsanitary conditions such as stagnant water, inadequate waste disposal, and unclean drainage systems provide breeding grounds for the vectors [5]. Environmental conditions that promote mosquito breeding contribute to the proliferation of Plasmodium species [6].

Transmission dynamics of malaria are influenced by a combination of climatic and anthropogenic factors that affect vector ecology and can increase transmission rates in certain areas [7]. Human behaviors and activities also play a role in human-vector contact and, consequently, affect the prevalence of malaria. Factors such as population demographics, environmental sanitation practices, and drainage patterns influence malaria prevalence [7].

Environmental attributes, including rainfall patterns, relative humidity, and temperature, are determinants that affect the ecology of malaria vectors [8]. Temperature, in particular, plays a significant role in the transmission dynamics of the vector and the growth and development of the parasite. The duration of extrinsic incubation, during which the parasite develops in the mosquito, is influenced by temperature. As temperatures rise, the feeding rate and blood digestion frequency of adult female Anopheles mosquitoes increase [7].

Malaria prevalence tends to be higher in rural areas compared to urban centers, which can be attributed to lifestyle factors. Iloh et al. [9] and Bassey and Nwakaku [10] reported that malaria is holoendemic in rural areas and mesoendemic in urban areas in Nigeria.

1.2 Causative agent

The causative agent of malaria is a group of parasites known as *Plasmodium*. These protozoan parasites belong to the Phylum Apicomplexa. Malaria in humans can be caused by several species of *Plasmodium*, with the most common and medically recognized species being *Plasmodium falciparum*, *Plasmodium malariae, Plasmodium vivax* and *Plasmodium ovale*.

The parasite *Plasmodium falciparum* is widely recognized as the most significant in terms of mortality. *Plasmodium falciparum* is responsible for inducing the most severe manifestation of malaria, frequently resulting in critical complications that pose a threat to an individual's life. The phenomenon is widespread in sub-Saharan Africa as well as certain regions across the globe.

Plasmodium vivax is a significant contributor to morbidity in various regions worldwide, and there is a growing body of evidence suggesting that mortality associated with this parasite has been underestimated [11]. This particular species is accountable for a substantial proportion of malaria cases on a global scale. Relapses may occur as a result of the emergence of dormant liver-stage parasites, known as hypnozoites, which have the ability to reactivate following a latent period. *Plasmodium vivax* exhibits a wide distribution in regions outside the African continent.

Plasmodium malariae is associated with chronic and milder malaria infections. It has a more limited geographic distribution compared to *P. falciparum* and *P. vivax*.

Plasmodium ovale is less common than other species but can cause relapses due to the presence of hypnozoites. It is mainly found in West Africa. *Plasmodium ovale curtisi*, *Plasmodium ovale wallikeri*, and *Plasmodium malariae* are infrequently encountered aetiological agents of clinically significant conditions. In recent times, the simian parasite *Pheidole knowlesi* has emerged as a significant local factor contributing to disease in Malaysia and other regions of southeast Asia. It is primarily a zoonosis, with no conclusive evidence supporting direct transmission from human to human [12].

1.3 Life cycle/transmission of the malaria parasite

Plasmodium species are widely distributed pathogens that exhibit an intricate life cycle involving female Anopheles mosquitoes and vertebrate hosts.

The complex life cycle of malaria parasites necessitates the expression of particular proteins in order to ensure their survival in both invertebrate and vertebrate hosts. These proteins are essential for intracellular and extracellular survival, making it possible for a variety of cell types to invade the body while dodging host immune responses. *P. ovale* and *P. vivax* sporozoites can either initiate immediate schizogony or undergo delayed schizogony as they pass through the aforementioned hypnozoite stage after being injected into the human host, in contrast to *P. falciparum* and *P. malariae* sporozoites. **Figure 1** shows the life cycle of the malaria parasite, which can be divided into several stages beginning with the entry of sporozoites into the bloodstream.

This life cycle necessitates the development of distinct zoite forms, which enable the invasion of specific cell types at particular stages. Upon entering the host, sporozoites proceed to invade hepatocytes, initiating the subsequent asexual replication cycle within the bloodstream. The sexual forms that arise during the blood stage are consumed by a mosquito during its feeding process, thereby concluding the life cycle.

1.4 In human host

Schizogony: The Anopheles mosquito bite, which introduces sporozoites into the human bloodstream, is what starts the human infection process. These tiny sporozoites set out for the liver, where they invade the cells of the liver. Once inside these hepatocytes, they go through a transformational process that causes them to develop

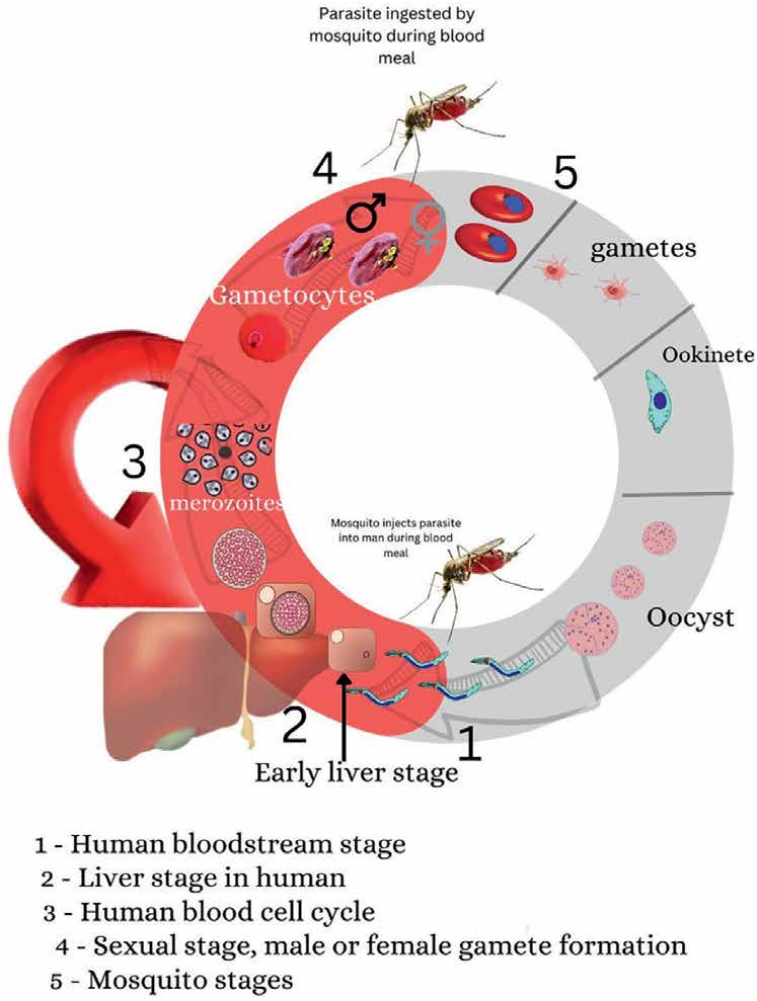

Figure 1.
Life cycle of plasmodium spp. in man.

into multi-nucleated structures called schizonts. These schizonts eventually burst, releasing merozoites, the next stage in the life cycle of the malaria parasite [13].

Intraerythrocytic Stage: The merozoites then start a crucial phase inside the host's bloodstream after being released. They invade erythrocytes, the red blood cells, and find refuge there. The merozoites undergo a different maturation process inside these erythrocytes, where they eventually turn into schizonts. As this maturation comes to a close, the schizont-infested erythrocytes burst, releasing a new wave of merozoites. The recurring fever episodes that distinguish malaria infections are brought on by this cycle [14].

Gametocyte Stage: Some of the merozoites undergo a remarkable transformation into male or female gametocytes, the sexual forms of the malaria parasite, as the infection progresses. Until a mosquito carrying the infection bites the host, these gametocytes are still present in the bloodstream. The gametocytes begin the next stage of the malaria life cycle after being ingested by the mosquito, leading to the development of sporozoites inside the insect that can then spread the disease to other people through bites [15].

1.5 Transition to mosquito

During successive cycles of schizogony within the bloodstream, a subset of parasites undergo a pivotal developmental transition that triggers their commitment to sexual development, leading to the formation of male and female gametocytes. The successful transmission of malaria from humans to mosquitoes is contingent upon the maturation of the sexual stages. This aspect has been acknowledged as a promising target for potential interventions, such as the utilization of transmission-blocking drugs or vaccines. However, it is known that the transition occurs during the preceding schizogony cycle, and that daughter merozoites originating from a single schizont-infected cell are predetermined to differentiate into either gametocytes or asexual schizonts. The presence of environmental stimuli, such as a high level of parasitemia and exposure to drugs like chloroquine, has been observed to be correlated with an elevated rate of conversion to gametocyte production. This suggests that parasites possess the ability to perceive and respond to their surroundings. The transportation of extracellular vesicles containing protein, RNA, and DNA between parasites in a controlled environment has been observed, indicating a mechanism for intercellular communication that enhances the production of gametocytes [16, 17]. The maturation of *P. falciparum* gametocytes is characterized by a prolonged duration compared to that of other species. After the initiation of commitment, the development of mature gametocytes that are capable of infecting mosquitoes requires a duration of 11 days. During this period, the parasites remain confined within the bone marrow [18], evading removal by the spleen until they eventually enter the peripheral circulation for an undetermined duration before being acquired by a mosquito during feeding.

1.6 In mosquito

Following a blood meal taken from an individual infected with malaria, a subsequent Anopheles mosquito becomes the carrier of this disease. During its feeding process, the mosquito ingests male microgametocytes and female macrogametocytes, both of which are transmitted through the initial mosquito's bite. Inside the mosquito's digestive tract, the fertilized gametocytes eventually unite, forming a zygote. This zygote then matures into an ookinete. As the ookinete progresses through the mosquito's gut wall, it transforms into an oocyst, which becomes populated with sporozoites. The oocyst, in turn, matures, ruptures, and liberates sporozoites. These sporozoites journey to the mosquito's salivary glands, awaiting their transfer to a human host during the insect's subsequent blood-feeding episode. This cyclical process thus initiates anew, perpetuating the malaria life cycle [19].

The life cycle of *Plasmodium vivax* quite different from that of *Plasmodium falciparum*. *P. vivax* parasites establish a dormant liver stage referred to as hypnozoites, which exhibit resistance to drugs targeting the erythrocytic stages. This unique feature complicates the eradication of *P. vivax*, as prevailing interventions struggle to counteract the dormant hypnozoites, leading to multiple relapses and the absence of effective treatments for this stage [20]. The life cycle of *Plasmodium* spp. is presented in **Figure 1**.

2. Pathogenesis

In the case of an individual with no previous exposure to malaria, infection typically results in the development of a feverish illness expressed as: abdominal

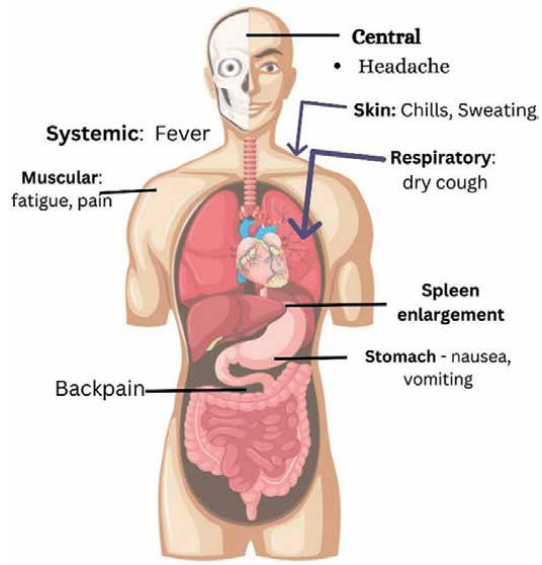

Figure 2.
Symptoms of malaria.

discomfort, headache, joint aches, muscle aches, vomiting, lethargy and anorexia [21]. The concomitant symptoms are nonspecific and frequently encompass rigors, cephalalgia, emesis, and myalgia (**Figure 2**).

If administered with suitable pharmaceutical interventions during this phase, the symptoms subside within a few days, albeit frequently accompanied by significant fatigue. In the context of *P. falciparum*, the administration of a comprehensive treatment regimen will result in the elimination of the infection. The reappearance of symptoms following treatment cessation can be attributed to inadequate treatment, drug resistance, or the occurrence of a new infection.

In instances involving *P. vivax* and *P. ovale*, recurring infections may transpire periodically due to the reactivation of the latent hypnozoite stage residing in the liver, unless it is eliminated through an extended course of treatment involving an 8-aminoquinolone medication. The comprehensive understanding of the progression of untreated or partially treated infection has been extensively documented through numerous observations conducted during the era when induced infections with both *P. falciparum* and *P. vivax* were employed as a therapeutic approach for neurosyphilis [22].

Typically, following a period of symptoms that may vary in intensity, the illness diminishes and the levels of parasites are effectively regulated at a minimal level. However, symptoms may reoccur periodically over the subsequent weeks and months, coinciding with increases in the presence of parasites in the bloodstream. Subsequent instances of parasitemia typically exhibit diminished intensity, resulting in less pronounced symptoms, ultimately leading to the resolution of the infection.

2.1 Severe malaria

In a subset of individuals who have not received adequate treatment or have received only partial treatment, the initial infection is not effectively managed and

advances to a severe or complicated form of malaria, potentially resulting in mortality. The depiction of severe malaria exhibits variations that are influenced by both age and transmission level, which in turn reflect the immune status of populations. The majority of malaria-related fatalities in Africa are observed in the pediatric population and are primarily characterized by three distinct syndromes, which can manifest either independently or concurrently: severe anemia, cerebral malaria, and respiratory distress [23]. Cerebral malaria can be operationally defined as the manifestation of a comatose state resulting from infection with the Plasmodium falciparum parasite. The clinical presentation described can be attributed to various factors and should not be equated with the histopathological characterization of cerebral malaria, which involves the accumulation of mature-infected parasites in the cerebral microvasculature [24]. The manifestation of respiratory distress in children afflicted with severe malaria is primarily characterized by metabolic acidosis, which predominantly arises as a consequence of tissue hypoxia. The destruction of both infected and uninfected red blood cells is commonly observed in cases of acute malaria infection. However, the occurrence of severe malarial anemia in young children is likely the result of a culmination of factors, including chronic anemia as a pre-existing condition, immune mechanisms, and ineffective erythropoiesis.

Severe malaria in older children and adults is infrequently observed in stably endemic regions of Africa due to the presence of naturally acquired immunity. Consequently, our comprehension of this syndrome in older individuals primarily relies on research conducted in regions with lower transmission rates, particularly in Asia. Severe malaria is typically characterized by the presence of cerebral malaria, hypoglycemia, and anemia. However, it is important to highlight that severe malaria is frequently observed as a multi-system disorder, often accompanied by notable renal and hepatic dysfunction. Such dysfunction is relatively uncommon in pediatric cases. Respiratory distress frequently arises as a consequence of pulmonary edema, a condition that is infrequently observed in pediatric patients but exhibits a significant fatality rate among adult individuals. As regions that were previously highly affected by a particular disease witness reductions in its transmission, resulting in a decrease in population immunity, there is an observable increase in the average age of individuals experiencing severe illness and death. Additionally, the nature of severe disease is shifting towards resembling the patterns observed in older patients in other global regions.

2.2 Interaction with other infections

Malaria presents a substantial obstacle to susceptible populations, particularly those who are exposed to multiple health hazards that frequently interact with each other. Co-infection with the human immunodeficiency virus (HIV) is a significant contributing factor that amplifies the gravity and mortality rate of malaria. According to van Eijk et al. [25], individuals of both pediatric and adult populations who are infected with HIV face an elevated susceptibility to severe illness and mortality as a result of malaria. Moreover, pregnant women afflicted with malaria exhibit an increased propensity to transmit the human immunodeficiency virus (HIV) to their fetuses, thereby exacerbating the health consequences for both the maternal and neonatal populations.

An additional significant interaction to be taken into account from a public health standpoint pertains to the correlation between malaria and invasive bacterial illnesses. The study conducted by Church and Maitland [26] reveals that there is a

higher prevalence of concurrent invasive bacterial diseases in African children suffering from severe malaria compared to what would be anticipated based on random chance. It is of utmost significance to note that individuals who are afflicted with dual infections exhibit a markedly elevated case fatality rate. Multiple mechanisms have been postulated to elucidate this correlation, encompassing the translocation of gram-negative microorganisms across a compromised intestinal barrier, distinct impairment of macrophages, and functional hyposplenism [27].

It is worth noting that according to Scott et al. [28], there is an estimation that malaria could potentially account for approximately 50% of inflammatory bowel disease (IBD) cases in specific geographical areas. This counterintuitive discovery implies that malaria may have an indirect impact on mortality rates that surpasses its direct effects. The notion is further supported by the significant decrease in childhood mortality rates that is observed during periods of intensive malaria control.

2.3 Malaria in pregnancy

In populations lacking immunity, the occurrence of malaria during pregnancy has been found to have a correlation with stillbirth and severe maternal illness, particularly with an increased susceptibility to hypoglycemia. In regions with high prevalence of malaria, where the local populations acquire a certain level of immunity, infection results in maternal anemia and reduced birth weight of the offspring [29]. While it is commonly referred to as a loss of immunity, it is important to note that this is not entirely accurate. Instead, the presence of the placenta provides a novel opportunity for parasites to sequester themselves by selectively binding to chondroitin sulfate A (CSA) on the syncytiotrophoblast [30].

2.4 Diagnosis

The Plasmodium parasite can be diagnosed using the following methods:

- The identification of malaria-specific antigens in the bloodstream through the utilization of rapid diagnostic tests (RDTs), OR
- The identification of parasite DNA that is specific to a particular species through the application of a Polymerase Chain Reaction (PCR) assay on a peripheral blood sample (Note: It is necessary for laboratory-developed malaria PCR tests to meet the requirements of the Clinical Laboratory Improvement Amendments [CLIA], which includes the completion of validation studies.) OR
- The identification of malaria parasites in thick or thin peripheral blood films, species determination based on morphological characteristics, and quantification of the proportion of red blood cells infected by asexual malaria parasites (parasitemia) are essential diagnostic approaches (**Figure 3**).

2.5 Treatment and management

The World Health Organization (WHO) has issued a recommendation for the use of antimalarial combination therapy in the treatment of uncomplicated falciparum malaria. This recommendation is in response to the growing concern over

Figure 3.
Thick blood smear for diagnosis of plasmodium parasite.

the development of resistance to monotherapies, which poses a significant threat to effective malaria treatment [31–33]. This refers to the concurrent administration of two or more blood schizonticidal drugs that possess distinct mechanisms of action and therefore target different biochemical pathways within the parasite. Artemisinin-based combination therapies (ACTs) are presently considered the primary treatment for uncomplicated falciparum malaria, as stated by the World Health Organization in 2021.

The treatment options for severe malaria consist of two categories of drugs administered intravenously: the cinchona alkaloids, which include quinine and quinidine, and the artemisinin monotherapies, which encompass artesunate, artemether, and artemotil. According to Piccoli et al. [34], during the period before the introduction of artemisinin-based combination therapies (ACTs), chloroquine demonstrated efficacy in the treatment of malaria caused by blood transfusion. Furthermore, due to the absence of an exoerythrocytic phase, the administration of tissue schizonticides like primaquine was deemed unnecessary. One particular case necessitated further intervention involving the administration of sulfadoxine-pyrimethamine and doxycycline in order to achieve the eradication of parasitemia and alleviate symptoms. Additionally, another patient received primaquine as part of their treatment regimen [35].

To relieve symptoms, avoid serious complications, and stop the spread of parasites that are resistant to medication, efficient treatment methods are essential. To treat this condition, a number of antimalarial medications have been created with various modes of action. It is significant to remember that different Plasmodium species, infection severity, patient age and health status, and the presence of drug resistance all affect treatment methods. Below is a **Table 1** showing different drugs used in treating malaria worldwide.

2.6 Prevention and control

The goal of controlling malaria has led to the implementation of a wide range of control methods. Different strategies have been adopted to combat the spread of diseases spread by vectors. These strategies include the use of insecticides, the destruction of disease vector breeding grounds and habitats, the use of insecticide-treated bed nets, indoor residual spraying, and targeted chemoprophylaxis [6]. Adefioye et al. [36] and other researchers have found that improving sanitation practices and raising public awareness have the potential to significantly reduce malaria incidence.

Insecticides have been widely used to get rid of or reduce the population of disease-carrying mosquitoes, to elaborate further on these tactics. The technique of

Drug class	Examples of drugs	Mechanism of action	Side effects
Chloroquine	Chloroquine, Hydroxychloroquine	Inhibits haeme polymerase, preventing haeme detoxification in parasites	Nausea, headache, blurred vision
Artemisinin-based Combination Therapies (ACTs)	Artemether-Lumefantrine, Artesunate-Mefloquine	Artemisinin disrupts parasite's intracellular calcium balance	Dizziness, vomiting, fever
Mefloquine	Mefloquine	Interferes with parasite's ability to metabolize haeme	Nausea, vomiting, dizziness
Quinine	Quinine	Interferes with parasite's ability to metabolize heme	Tinnitus, blurred vision, nausea
Atovaquone-Proguanil	Atovaquone-Proguanil	Disrupts mitochondrial electron transport chain	Nausea, abdominal pain, rash
Primaquine	Primaquine	Targets dormant liver stage (hypnozoites) of P. vivax	Haemolysis in G6PD-deficient individuals

Table 1.
Drugs used in treating malaria worldwide.

indoor residual spraying involves applying insecticides to the interior walls of buildings to kill mosquitoes immediately upon contact. According to Okonko et al. [6], this strategy has shown promise in lowering disease transmission rates by reducing vector populations.

Targeting breeding grounds and habitats for vectors has also proven essential in stopping the life cycle of disease-carrying insects. Eliminating sources of stagnant water where mosquitoes can breed will stop their spread, which will reduce the likelihood of disease transmission. In addition, using bed nets treated with insecticide is now essential to preventing malaria. These nets protect people while they sleep, which is when mosquitoes are most active and feeding, by either repelling or killing any that come into contact with them.

Chemoprophylaxis is a strategy that involves giving medication to people in high-risk areas in an effort to stop the disease from spreading. In areas with a high malaria prevalence, this proactive approach has been especially helpful. The work of Adefioye et al. [36] highlights the importance of societal factors in malaria control in addition to medical interventions. Their findings highlight the significance of promoting better sanitation practices and educating the public about preventive measures, both of which can make a significant difference in the burden of the disease.

In a broader sense, community involvement and cooperation between governmental, medical, and non-governmental organizations are essential to the effective application of these strategies. A multi-pronged approach to malaria control emerges through the integration of scientific research, targeted interventions, and a thorough understanding of local contexts, showing promising potential to eventually eliminate the prevalence and impact of the disease.

2.7 Current status

Despite the implementation of extensive control and elimination measures at both international and national levels through malaria control programs, malaria remains the predominant parasitic disease worldwide. The Global Malaria Eradication

Program, which began in 1969, failed to achieve its objectives, resulting in millions of people contracting malaria, primarily in sub-Saharan Africa. The disease claimed the lives of tens of millions, particularly affecting pregnant women who faced malaria-related complications during childbirth. Additionally, millions of children were born with low birthweight, leading to early mortality or disability [1].

However, the first two decades of the 21st century have been regarded as a significant period in malaria control efforts [1]. According to the latest annual global malaria report released by the World Health Organization (WHO), approximately 229 million malaria cases were estimated in 2019 across 87 countries where malaria is endemic. This figure represents a decrease of 9 million cases from the year 2000, but it remains higher than the 218 million estimated cases reported in 2015 as part of the Global Technical Strategy (GTS) for malaria 2016–2030 [1].

The decline in global malaria case incidence, measured as the number of cases per 1000 people at risk, demonstrates this trend. From 80 cases in 2000, the incidence dropped to 58 in 2015 and further to 57 in 2019. This signifies a 27% reduction between 2000 and 2015, followed by a less than 2% decline between 2015 and 2019, indicating a slower rate of decrease since 2015.

In Africa, the majority of malaria infections are caused by the highly virulent P. falciparum parasite, which also accounts for the majority of malaria-related deaths globally. However, the prevalence of P. vivax infections, particularly in the Indian subcontinent, presents distinct challenges in terms of diagnosis and treatment [37]. In 2019, *P. falciparum* malaria comprised almost 99% of cases in Africa and 94% of all malaria cases and deaths worldwide [1].

2.8 Future perspectives

At present, there is no available vaccine for malaria. However, it is widely recognized that the development of new tools, including vaccines, is crucial for maintaining the progress made in disease control and advancing towards the elimination and eventual eradication of malaria. Over the past three decades, efforts to develop vaccines have targeted various stages of the malaria parasite, including the pre-erythrocytic (sporozoite and liver stages), blood stages, and sexual stages.

Malaria would be halted by a highly effective pre-erythrocytic vaccine that prevented the development of blood-stage infection. It has been thought that vaccinations against the blood stages that reproduce asexually are crucial for lowering morbidity and mortality. The transmission cycle would be broken by vaccines that target the sexual stages, but an infection that has already taken hold inside the vaccinated person would not be directly impacted. Based on the bottleneck hypothesis, vaccine development efforts shifted towards the pre-erythrocytic and sexual stages as the idea of elimination gained popularity. In contrast to replicating blood stages, which are more numerous and have developed immune evasion mechanisms for long-term survival, this hypothesis suggests that targeting the numerical bottlenecks in parasite development, such as the injected sporozoites prior to liver invasion and the mosquito midgut transmission stages, would result in higher vaccine effectiveness. The problem with this strategy is that the pathogenic replicative cycle can continue if one sporozoite or ookinete manages to evade the vaccine. Additionally, it appears that the immunity developed against these particular targets is strictly stage-specific [38].

As we progress towards elimination, this challenge becomes even more critical. A combination of population loss of naturally acquired blood-stage immunity, waning vaccine efficacy, and the presence of drug-resistant strains could create a dangerous

situation for the resurgence of malaria transmission. The ideal malaria vaccine would be based on conserved targets that provide lifelong sterile protection from an early age with minimal doses. However, achieving this ideal has proven elusive thus far [31–33].

The most advanced candidate vaccine in clinical development is RTS,S/AS01, which targets the sporozoite stage. This vaccine has undergone phase III clinical trials involving over 15,000 African children and serves as the benchmark against which future vaccines will be evaluated. After 1 year of follow-up, a three-dose series of RTS,S/AS01 reduced clinical malaria cases by 28% in young children and 18% in infants. However, a notable finding from these trials is the relatively short duration of protection, highlighting the need to investigate the underlying reasons [39].

Known also as Mosquirix, the RTS,S/AS01 vaccine is a ground-breaking weapon in the fight against malaria. It is intended to prevent Plasmodium falciparum malaria, the most dangerous form of the illness, and is the first malaria vaccine in the entire world to receive regulatory approval. The PATH Malaria Vaccine Initiative and other partners assisted GlaxoSmithKline (GSK) in developing the vaccine.

Vaccine Composition and Mechanism of Action: Recombinant proteins are the basis of the RTS,S/AS01 vaccine. It combines a portion of the hepatitis B surface antigen with the circumsporozoite protein (CSP) of Plasmodium falciparum. The 3-O-desacyl-4′-monophosphoryl lipid A (MPL) and QS-21, a saponin derivative, are two immunostimulants that are included in the AS01E adjuvant, a liposome-based formulation that is part of the adjuvant system used in the vaccine formulation. The effectiveness of the vaccine is increased by the adjuvant system, which improves the immune response.

The CSP found on the sporozoite stage of the malaria parasite is the target of the vaccine's immune response, which is how it works. Following vaccination, a person's immune system responds to the CSP antigen by recognizing it. In order to stop the parasites from progressing to the blood stage of infection and causing clinical malaria, this immune response aims to neutralize the sporozoites and infected liver cells.

Clinical Trials and Efficacy: The RTS,S/AS01 vaccine was developed after extensive clinical trials were carried out in several malaria-endemic African nations. The efficacy of the vaccine in lowering the incidence of malaria in young children and infants was demonstrated in the Phase 3 clinical trial, also known as the RTS,S Clinical Trials Partnership [31–33].

The trial's findings showed that the vaccine only partially protected against malaria. The vaccine demonstrated efficacy against clinical malaria and severe malaria anemia in infants, and it significantly decreased the number of severe malaria cases in young children. However, the vaccine's efficacy gradually decreased, necessitating booster doses to continue providing protection [31–33].

Implementation and Ongoing Research: The World Health Organization (WHO) advised the use of the RTS,S/AS01 vaccine in pilot implementation programmes in a few African nations with high malaria burdens after regulatory approval. These pilot projects aimed to assess the vaccine's practical application, viability, and efficacy in a larger population [31–33].

Over the next 2 years, the first-ever malaria vaccine will be administered to 18 million people in 12 different African countries and regions. The rollout represents a significant advance in the fight against one of the continent's leading causes of death [40].

The doses have been prioritized to areas with the greatest need, where the risk of malaria illness and death among children is highest, using the principles outlined in the Framework for allocation of limited malaria vaccine supply [40].

The Malaria Vaccine Implementation Programme (MVIP), coordinated by WHO and funded by Gavi, the Vaccine Alliance, the Global Fund to Fight AIDS, Tuberculosis and Malaria, and Unitaid, has been providing the malaria vaccine to Ghana, Kenya, and Malawi since 2019. Since its administration to more than 1.7 million kids in Ghana, Kenya, and Malawi in 2019, the RTS,S/AS01 vaccine has been proven to be both safe and effective, leading to a significant decline in both severe malaria and child mortality. The malaria vaccine has attracted interest from at least 28 African nations [40].

Nine additional nations, including Benin, Burkina Faso, Burundi, Cameroon, the Democratic Republic of the Congo, Liberia, Niger, Sierra Leone, and Uganda, will be able to incorporate the vaccine into their routine immunization programmes for the first time thanks to the initial 18 million dose allocation, in addition to Ghana, Kenya, and Malawi. This distribution round makes use of the vaccine doses that Gavi, Vaccine Alliance has access to through UNICEF. The first doses of the vaccine should arrive in countries in the final quarter of 2023, and they should begin to be distributed by early 2024 [40].

Research is still being conducted to evaluate the vaccine's long-term effects, ideal dosing regimens, and potential integration into current malaria control strategies as a result of its use in real-world settings. Additionally, researchers are examining how well the vaccine works in various age groups and how it interacts with other malaria interventions like insecticide-treated bed nets and antimalarial drugs.

A thorough investigation of the interactions between malaria parasites and the human immune system, as well as their co-evolution, is urgently needed in order to develop better vaccine strategies. Additionally, early-stage clinical trials of a radiation-attenuated whole-cell sporozoite vaccine (PfSPZ) have demonstrated promise in offering sterile protection against homologous challenge. The lack of demonstrated heterologous (cross-strain) protection, the need for a large number of parasites and intravenous administration to induce anti-sporozoite immunity, and the logistical difficulty of preserving the vaccine's viability with a liquid nitrogen cold chain are just a few of this vaccine's significant drawbacks. The fundamental problem of inducing strain-transcendent protection, which remains a top priority in vaccine development, is still present in other live-cell sporozoite vaccine approaches, such as genetically attenuated parasites and chemoprophylaxis with sporozoites [14]. These approaches may offer incremental improvements over PfSPZ.

3. Conclusion

The majority of malaria cases and deaths are concentrated in sub-Saharan African and south/southeast Asian countries. However, there are instances of imported malaria cases in regions considered malaria-free or that have recently achieved malaria eradication through dedicated efforts. This emergence of imported malaria cases in non-endemic areas poses a new public health challenge. Particularly, imported cases from South Asia, where *P. vivax* infections are prevalent, can lead to the persistence of dormant liver-stage hypnozoites, causing recurrent episodes of malaria in non-endemic settings. If suitable breeding environments for mosquito

vectors, such as construction sites with artificial water reservoirs, are present, imported *P. vivax* infections can result in local outbreaks.

Factors like global warming, increased travel for business or leisure purposes, migration due to employment opportunities or geopolitical conflicts, and changes in land use (such as plantation drives in previously barren areas) have altered the epidemiological characteristics of imported malaria in various countries. If not managed properly, these conditions can elevate vector density levels to the point where local transmission of the disease may occur following imported malaria cases. The rise of drug-resistant malaria, particularly drug-resistant strains of *P. vivax*, poses a significant threat to malaria control efforts in malaria-free countries with a substantial number of expatriates originating from *P. vivax*-endemic regions. Therefore, regular monitoring of imported malaria cases is essential in such settings.

To maintain malaria-free status, non-endemic countries must adhere to measures such as early diagnosis, appropriate treatment, integrated mosquito control programs, and consistent monitoring of drug resistance in Plasmodium species. Additionally, the adoption of efficient and effective vector control measures is crucial in preventing imported malaria cases from leading to indigenous transmission in many countries. Continuous efforts and vigilance are necessary to sustain the status of being malaria-free in these regions.

Author details

Talabi Helen Bamikole
Western Delta University, Delta State, Oghara, Nigeria

*Address all correspondence to: bamikolehelenrarebird@gmail.com

IntechOpen

References

[1] World Health Organisation. World Malaria Report. Geneva, Switzerland. Available from: https://www.who.int/publications/i/item/9789240015791: WHO; 2020 [Accessed: December 8, 2020]

[2] Ojo DA, Mafiana CF. Prevalence of malaria and typhoid infections in endemic community of Ogun state, Nigeria. Bioscience and Biotechnology Research Asia. 2005;**3**(1):9-16

[3] Ani OC. Endemicity of malaria among primary school children in Ebonyi state, Nigeria. Animal Research International. 2004;**1**(3):155-159

[4] Nasir IA, Muhammad MA, Emeribe AU, Babayo A, Shehu MS. Prevalence of malaria parasitaemia among residents proximal to environmental waste dumpsites in Gwagwalada metropolis, Abuja, Nigeria. Journal of Medicine in the Tropics. 2015;**17**(2):91-96

[5] Pam VA, Landan S, Pam DD, Gullek JF, Okoro J, Ogbu KI, et al. The prevalence of malaria and typhoid co-infection in pregnant women attending antenatal in Wuse general hospital Abuja, Nigeria. Scientific Journal of Veterinary Advances. 2015;**4**(6):39-50

[6] Okonko IO, Donbraye-Emmanuel OOB, Donbraye E, Abubakar MJ, Fowotade A, Fadeyi A, et al. Malaria parasitaemia among patients in Ibadan, Southwestern Nigeria. Journal of Applied Biosciences. 2010;**29**:1774-1780

[7] Ukpong IG, Etim SE, Ogban EI, Abua LL. Prevalence of malaria in the highlands of Obudu cattle ranch, Nigeria. International Journal of Tropical Disease and Health. 2015;**7**(3):87-93

[8] Alaba OA, Alaba OB. Malaria in rural Nigeria: Implications for the millennium development goals. African Development Review. 2009;**21**(1):73-85

[9] Iloh GUP, Orji UN, Amadi AN. Malaria morbidity among under-five Nigerian children: A study of its prevalence and health practices of primary care givers (mothers) in a resource-poor setting of a rural hospital in Eastern Nigeria. European Journal of Preventive Medicine. 2013;**1**(3):50-57

[10] Bassey SE, Nwakaku IL. Prevalence of malaria parasitaemia among children between 1-10 years old attending Federal Medical Centre, Yenagoa, Bayelsa state, Nigeria. EC Pharmacology and Toxicology. 2017;**3**(2):43-48

[11] Naing C, Whittaker MA, Nyunt Wai V, Mak JW. Is *Plasmodium vivax* malaria a severe malaria?: A systematic review and meta-analysis. PLoS Neglected Tropical Diseases. 2014;**8**:e3071

[12] Ahmed MA, Cox-Singh J. *Plasmodium knowlesi* - an emerging pathogen. ISBT Science Series. 2015;**10**(1):134-140

[13] Yamauchi LM, Coppi A. Malaria: Liver Stages. In: Encyclopedia of Malaria. Cham: Springer; 2019. pp. 1-7. DOI: 10.1007/978-3-319-90188-3_111-1

[14] Cowman AF, Healer J, Marapana D, Marsh K. Malaria: Biology and disease. Cell. 2016;**167**(3):610-624

[15] Bousema T, Drakeley C. Epidemiology and infectivity of *Plasmodium falciparum* and *Plasmodium vivax* gametocytes in relation to malaria control and elimination. Clinical Microbiology Reviews.

2011;**24**(2):377-410. DOI: 10.1128/CMR.00051-10

[16] Mantel PY, Hoang AN, Goldowitz I, Potashnikova D, Hamza B, Vorobjev I, et al. Malaria-infected erythrocyte-derived microvesicles mediate cellular communication within the parasite population and with the host immune system. Cell Host & Microbe. 2013;**13**:521-534

[17] Regev-Rudzki N, Wilson DW, Carvalho TG, Sisquella X, Coleman BM, Rug M, et al. Cell-cell communication between malaria-infected red blood cells via exosome-like vesicles. Cell. 2013;**153**:1120-1133

[18] Joice R, Nilsson SK, Montgomery J, Dankwa S, Egan E, Morahan B, et al. *Plasmodium falciparum* transmission stages accumulate in the human bone marrow. Scientific Translations in Medicine. 2014;**6**:244-245

[19] Centers for Disease Control (CDC). Malaria: Biology. Georgia: US Centers for Disease Control (CDC); 2010. Update. Available from: www.cdc.gov/malaria/about/biology/index.html

[20] Westenberger S, McClean C, Chattopadhyay R, Dharia N, Carlton J, Barnwell J. A systems-based analysis of *Plasmodium vivax* lifecycle transcription from human to mosquito. PLoS Neglected Tropical Diseases. 2010;**4**(4):653

[21] Sabina K. Prevalence and epidemiology of malaria in Nigeria: A review. International Journal of Research in Pharmacy and Biosciences. 2017;**4**(8):10-12

[22] Collins WE, Jeffery GM. A retrospective examination of sporozoite- and trophozoite-induced infections with *Plasmodium falciparum*: Development of parasitologic and clinical immunity during primary infection. American Journal of Tropical Medicine and Hygiene. 1999;**61**:4-19

[23] Marsh K, Forster D, Waruiru C, Mwangi I, Winstanley M, Marsh V, et al. Indicators of life-threatening malaria in African children. New England Journal of Medicine. 1995;**332**:1399-1404

[24] Taylor TE, Molyneux ME. The pathogenesis of pediatric cerebral malaria: Eye exams, autopsies, and neuroimaging. Annals of the New York Academy of Sciences. 2015;**1342**:44-52

[25] van Eijk AM, Ayisi JG, Ter Kuile FO, Slutsker L, Shi YP, Udhayakumar V, et al. HIV, malaria, and infant anaemia as risk factors for postneonatal infant mortality among HIV-seropositive women in Kisumu, Kenya. The Journal of Infectious Diseases. 2007;**196**:30-37

[26] Church J, Maitland K. Invasive bacterial co-infection in African children with *Plasmodium falciparum* malaria: A systematic review. BMC Medicine. 2014;**12**:31

[27] Gomez-Perez GP, van Bruggen R, Grobusch MP, Dobano C. *Plasmodium falciparum* malaria and invasive bacterial co-infection in young African children: The dysfunctional spleen hypothesis. Malaria Journal. 2014;**13**:335

[28] Scott JA, Berkley JA, Mwangi I, Ochola L, Uyoga S, Macharia A, et al. Relation between falciparum malaria and bacteraemia in Kenyan children: A population-based, case-control study and a longitudinal study. Lancet. 2011;**378**:1316-1323

[29] McLean AR, Ataide R, Simpson JA, Beeson JG, Fowkes FJ. Malaria and immunity during pregnancy and postpartum: A tale of two species. Parasitology. 2015;**142**:999-1015

[30] Khunrae P, Dahlback M, Nielsen MA, Andersen G, Ditlev SB, Resende M, et al. Full length recombinant *Plasmodium falciparum* VAR2CSA binds specifically to CSPG and induces potent parasite adhesion-blocking antibodies. Journal of Molecular Biology. 2010;**397**:826-834

[31] WHO. Malaria vaccine: WHO position paper – January 2021. Weekly Epidemiological Record. 2021;**96**(4):29-52

[32] World Health Organisation (WHO). Guidelines for the Treatment of Malaria. 3rd ed. Geneva: WHO; 2021

[33] World Health Organisation. Malaria. Geneva: WHO; 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/malaria

[34] Piccoli DA, Perlman S, Ephros M. Transfusion acquired *Plasmodium malariae* infection in two premature infants. Pediatrics. 1983;**72**:560-562

[35] Joishy SK, Lopez CG. Transfusion induced malaria in a splenectomized β-thalassemia major patient and review of blood donor screening methods. American Journal of Hematology. 1980;**8**:221-229

[36] Adefioye OA, Adeyeba OA, Hassan WO, Oyeniran OA. Prevalence of malaria parasite infection among pregnant women in Osogbo, Southwest, Nigeria. American-Eurasian Journal of Scientific Research. 2007;**2**(1):43-45

[37] Dayananda KK, Achur RN, Gowda DC. Epidemiology, drug resistance, and pathophysiology of *Plasmodium vivax* malaria. Journal of Vector Borne Diseases. 2018;**55**:1-8

[38] Seder RA, Chang LJ, Enama ME, Zephir KL, Sarwar UN, et al. VRC 312 Study Team. Protection against malaria by intravenous immunization with a nonreplicating sporozoite vaccine. Science. 2013;**341**:1359-1365

[39] Spring M, Murphy J, Nielsen R, Dowler M, Bennett JW, Zarling S, et al. First-in-human evaluation of genetically attenuated *Plasmodium falciparum* sporozoites administered by bite of anopheles mosquitoes to adult volunteers. Vaccine. 2013;**31**:4975-4983

[40] World Health Organization. 18 Million Doses of First-Ever Malaria Vaccine Allocated to 12 African Countries for 2023-2025: Gavi, WHO and UNICEF. Geneva: WHO; 2023

Chapter 3

Chagas Disease: A Review of the Disease and Its Interaction with COVID-19

Diego-Abelardo Álvarez-Hernández, Daniella Pinto, Luis Martínez-Juárez, Rodolfo García-Rodríguez-Arana and Alejandra Montoya

Abstract

Chagas disease is a chronic and silent disease caused by *Trypanosoma cruz*i. It is endemic to Latin America, but it has spread to non-endemic countries worldwide. It is primarily a vector-borne disease that is transmitted by triatomines. It has a broad clinical spectrum and infected individuals can develop life-threatening complications if left undiagnosed and remain untreated. COVID-19 is a complex and evolving disease caused by SARS-CoV-2. It has caused a catastrophic global effect, infecting about 768 million people, of which almost 200 million live in America, where both diseases overlap. The resources that have been assigned to fight back its burden have disrupted essential health services that are needed to advance towards the control, elimination, and eradication of Chagas disease. This chapter includes an overview of the disease, discusses its interaction with COVID-19, and highlights the crucial priorities for healthcare professionals and policymakers to leave no one behind.

Keywords: American trypanosomiasis, Chagas disease, COVID-19, Neglected Tropical Diseases, *Trypanosoma cruzi*

1. Introduction

Chagas disease is a chronic and silent disease caused by *Trypanosoma cruzi*, an intracellular protozoan that is mainly transmitted by the bite of infected triatomines. It is endemic to Latin America, but cases have been increasing significantly in non-endemic countries, making it a global health issue [1]. When acquired, the disease develops in stages. During the acute stage, most people remain asymptomatic, meanwhile, during the chronic stage, some people develop cardiovascular and gastrointestinal complications. Delayed diagnosis and inadequate treatment decrease their life quality and increase their risk of death. Up to date, awareness is the best option for prevention. There is no preventive or therapeutic vaccine available [1, 2]. Although it has been historically neglected, the Coronavirus Disease 19 (COVID-19) pandemic has worsened the situation, especially for Neglected Tropical Diseases (NTDs),

which mainly affect impoverished and marginalized populations. Awareness and advocacy campaigns were discontinued, access and quality of healthcare were limited or inconsistent, control and surveillance programs were disrupted, and research and development were paused or slowed down [3, 4].

2. Epidemiology

2.1 Background

Chagas disease is one of twenty NTDs that have been recognized by the World Health Organization. They are common in tropical and subtropical regions, where adequate climate conditions enable their transmission. NTDs are intimately linked to communities in which disparities and inequities prevail. When acquired, they cause disabilities and suffering, but they also lead to discrimination and stigmatization, excluding people from their role in their societies. In this context, Chagas disease is the most common NTD in Latin America, but it is increasingly raising worldwide [2, 3].

2.2 Endemic countries

Chagas disease is endemic to Latin America (Central and South America), where it is estimated that there are about 6 million infected people, but almost 65 million are at risk of becoming infected. Endemic countries include Argentina, Belize, Bolivarian Republic of Venezuela, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Guiana, French Guiana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Plurinational State of Bolivia, Surinam, and Uruguay. Each year approximately 30,000 new cases and around 12,000 deaths are reported. Besides, its annual burden is estimated in 6.2 billion dollars for endemic countries [5, 6].

2.3 Non-endemic countries

Chagas disease has become a global health issue, as it has spread to non-endemic countries, where it is estimated that there are around 400,000 infected people, but at least 32 million immigrants from endemic countries should be screened. It has been reported in North America (Canada and the United States of America), Asia (Japan), Europe (Austria, Belgium, Croatia, Denmark, France, Luxembourg, Italy, Netherlands, Norway, Portugal, Romania, Sweden, Spain, Switzerland, and the United Kingdom), and Oceania (Australia and New Zealand). Climate change and migration are the main reasons for its spread. Furthermore, its annual burden is estimated in 1 billion dollars for non-endemic countries [6, 7].

3. Etiology and transmission

3.1 Taxonomy

Chagas disease is caused by a parasite that belongs to the class *Kinetoplastea*, order *Trypanosomatida*, family *Trypanosomatidae*, genus *Trypanosoma*, and species *cruzi* [8].

3.2 Lineages

T. cruzi is an intracellular obligate parasite with genetic heterogeneity. It has been classified into six discrete typing units (DTUs) or lineages (TcI to TcVI). Each of them has its distribution, ecology, and pathogenicity [9].

3.3 Vector-borne transmission

It is primarily a vector-borne disease. When an infected triatomine has a blood meal from a non-infected host, it defecates and releases metacyclic trypomastigotes. Metacyclic trypomastigotes enter through the bite site to reach phagocytic and non-phagocytic cells in the subcutaneous tissues, where they bind to a parasitophorous vacuole, differentiate into amastigotes, escape the parasitophorous vacuole, and replicate in the cytoplasm by binary fission. Then, amastigotes differentiate into bloodstream trypomastigotes, induce lysis of the cell membrane, and travel through the blood vessels to infect new cells. When a non-infected triatomine has a blood meal from an infected host, it ingests blood trypomastigotes. Blood trypomastigotes migrate through the gastrointestinal tract to reach the stomach and midgut, where they differentiate into epimastigotes and replicate by binary fission. Then, epimastigotes migrate towards the hindgut, attach to peri microvillar membranes, differentiate into metacyclic trypomastigotes, travel to the rectum, and adhere to the epithelium to be ready to infect new non-infected hosts (**Figure 1**) [10, 11]. Other morphological forms have been described elsewhere [11].

3.4 Non-vector-borne transmission

Chagas disease can also be acquired by blood transfusion or organ transplantation from an infected donor to a non-infected receptor, during pregnancy or childbirth from an infected mother to a non-infected fetus or newborn (congenital or vertical transmission), by consuming beverages or food contaminated with the feces of an infected triatomine (oral transmission), or by having contact with contaminated

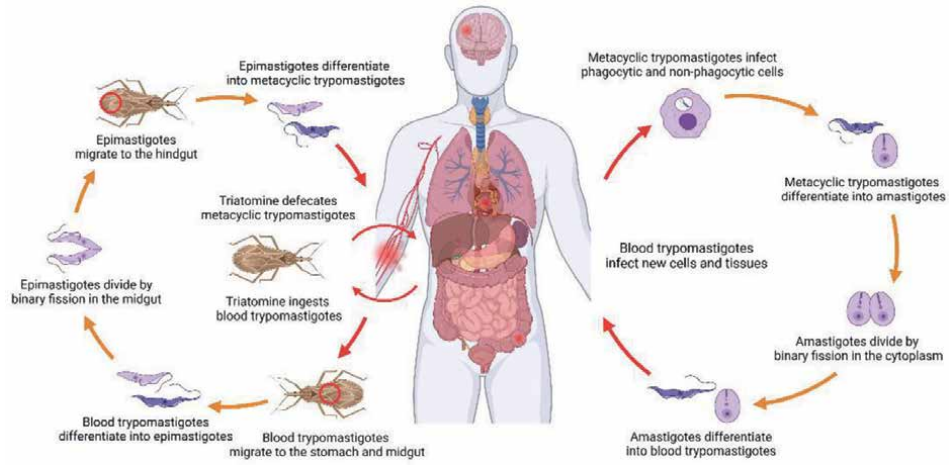

Figure 1.
Trypanosoma cruzi life cycle. Created with BioRender.com.

blood or tissue samples at the laboratory or hospital (accidental or occupational transmission) [1, 12].

4. Risk factors

Lack of awareness, living or visiting endemic countries, being exposed to triatomines and their reservoirs, and poor-quality housing are the main risks for acquiring the disease [2, 13].

5. Clinical manifestations

5.1 Incubation

Chagas disease has an incubation period that ranges from 7 to 14 days if the infection was acquired by vector-borne transmission and from 3 to 120 days if it was acquired by non-vector-borne transmission (3 to 22 days for oral transmission and 90 to 120 days for blood transfusion and organ transplantation). Then, the disease develops into stages: [14, 15].

5.2 Acute stage

95% of the infected individuals remain without clinical manifestations. The other 5% can develop fever, fatigue, weakness, myalgia, arthralgia, headache, nausea, vomiting, abdominal pain, hepatomegaly, and splenomegaly. Seldomly, a painful mobile nodule can arise at the inoculation site when the parasite load is high (chagoma), and a unilateral painless palpebral swelling can be seen when the parasite enters through the mucous membrane of the eye (Romaña's sign). Rarely, meningoencephalitis, myocarditis, or pericardial effusion can develop, especially if there is immunosuppression or when the infection was acquired by oral transmission. The duration of the acute stage ranges from 120 to 240 days [14, 15].

5.3 Chronic stage

70 to 90% of the infected individuals establish in the chronic indeterminate stage, in which they have a positive serology for *T. cruzi*, but remain without clinical manifestations. The other 10 to 30% can develop the chronic determinate stage, in which they have a positive serology for *T. cruzi* and experience the clinical manifestations of the cardiac and digestive forms: [14, 15].

5.3.1 Cardiac form

It causes damage to the cardiac conduction system and generates a classical dilated cardiomyopathy that leads to arrhythmias, heart failure, and pulmonary thromboembolism. Infected individuals with arrythmias can experience anxiety, dizziness, syncope, dyspnea, bradycardia, tachycardia, palpitations, and chest pain. Infected individuals with heart failure can experience anxiety, fatigue, weakness, hyporexia, anorexia, nausea, vomiting, dyspnea, paroxysmal nocturnal dyspnea, orthopnea, bendopnea, chronic and persistent cough, bradycardia, tachycardia, palpitations, chest

pain, and edema. Infected individuals with pulmonary thromboembolism can experience anxiety, confusion, dizziness, syncope, dyspnea, tachypnea, hemoptysis, and chest pain that worsens when breathing or coughing. Cardiac sudden death occurs in 50 to 60% of the cases [14, 15].

5.3.2 Digestive form

It causes damage to the enteric nervous system and generates dilatation and dysfunction of the smooth muscle that leads to megaesophagus and megacolon. Infected individuals with megaesophagus can experience weight loss, hyporexia, anorexia, nausea, vomiting, odynophagia, dysphagia, achalasia, pyrosis, regurgitation, bronchoaspiration, and chronic and persistent cough. Infected individuals with megacolon can experience weight loss, hyporexia, anorexia, nausea, vomiting, abdominal pain, abdominal distention, constipation, fecaloma, volvulus, and bowel ischemia [14, 15].

5.3.3 Reactivation

It occurs when infected individuals that are at the chronic stage become immunocompromised due to immunodepression or immunosuppression, allowing the parasite's reactivation and replication. It can cause life-threatening meningoencephalitis, myocarditis, or panniculitis [14, 15].

6. Diagnosis

6.1 Background

Chagas disease must be suspected when people that live or visit endemic countries experience the above-mentioned clinical manifestations, but it should be confirmed with laboratory tests, which depend upon the stage of the disease: [16].

6.2 Acute stage

Direct examination of the blood trypomastigotes in a fresh or stained blood smear with conventional microscopy is the gold standard for diagnosis. Concentration techniques can be employed if the level of parasitemia is low, and multiple samples should be obtained to improve the chances of detection. It is a cheap and simple test that can be performed in adequately equipped laboratories with highly trained technicians. Other tests that can be employed for parasitological observation are hemoculture, in which a blood sample is collected, cultured, and incubated, and xenodiagnoses, in which a blood sample is collected and given to a non-infected triatomine. Both allow the exponential growth of the parasites and have an improved sensitivity, but consume plenty of time. Hence, they have been displaced and disused. Detection of the genetic material of *T. cruzi* in a blood sample can be done with a Polymerase Chain Reaction (PCR), in which the DNA is extracted, amplified, and detected. It can be employed if the level of parasitemia is low. Its results are highly sensitive and specific and can be performed in adequately equipped laboratories with highly skilled technicians. However, it is expensive. Therefore, although it is a desired laboratory study, it is not available in remote settings that lack resources [16, 17].

6.3 Chronic stage

Detection of the antibodies against *T. cruzi* in a blood sample with an Enzyme-Linked Immunosorbent Assay (ELISA), Indirect Hemagglutination Assay (IHA), Indirect Immunofluorescence Assay (IFA), or Western Blot (WB) is the gold standard for diagnosis. However, as they are moderately sensitive, the Pan American Health Organization (PAHO) and the WHO have established that at least two different serological tests with different principles must be employed to obtain reliable results. If both are positive, then it is a conclusive diagnosis, but if one of them is negative and the other is positive, then a third serological test should be used. All require adequately equipped laboratories with highly trained technicians, but ELISA is the most cost-effective and easy to perform. IFA is more sensitive and specific than IHA, and WB is mainly used for research [16, 17].

6.4 Complimentary examination

Cabinet and imaging studies must be employed to assess cardiac and digestive involvement: [14].

6.4.1 Cardiovascular tests

Chest X-rays, electrocardiography, and echocardiography should be performed, according to the available resources and the index of suspicion if the infected individual experiences cardiac clinical manifestations. Cardiomegaly and pulmonary congestion can be detected in chest X-rays. Conduction disorders (first, second, or third atrioventricular block, complete and incomplete right bundle branch block plus left anterior fascicular block, and isolated left anterior fascicular block), bradyarrhythmia's (sinus bradycardia), and tachyarrhythmias (atrial fibrillation, frequent and isolated polymorphic premature ventricular contractions, and non-sustained ventricular tachycardia) can be identified in the electrocardiogram. Abnormalities in the cardiac valves (mitral and tricuspid regurgitation), in the motion of the segmental wall (hypokinesia, dyskinesia, or akinesia in the apical and inferolateral walls), in the function of the ventricles (left and right ventricular dilation with systolic and diastolic dysfunction), apical aneurysms and mural thrombosis can be observed in the echocardiogram [14, 15].

6.4.2 Gastrointestinal tests

Barium esophagram, upper endoscopy, barium cologram, and lower endoscopy should be performed, according to the available resources and the index of suspicion if the infected individual experiences digestive clinical manifestations. Megaesophagus (dilation of the esophagus, impaired peristalsis, and esophageal stasis) can be seen in the barium esophagram and the upper endoscopy. Megacolon (dilation of the colon, impaired peristalsis, fecaloma, and volvulus) can be spotted in the barium enema and lower endoscopy [14, 18].

7. Treatment

7.1 Trypanocides

Chagas disease can be treated with benznidazole or nifurtimox. Both have activity against *T. cruzi*, but their efficacy depends upon the stage of the disease. Therefore, the

PAHO and the WHO encourage their use for infected individuals who are at the acute stage or at the chronic indeterminate stage, in which the benefits of giving them outweigh the risks of prescribing them, and discourage their use for infected individuals who are at the chronic determinate stage, in which specific organ damage has already developed. Both have their contraindications, dosage regimen, and adverse effects: [17, 19].

7.1.1 Benznidazole

It is absolutely contraindicated during pregnancy and in case of severe hepatic failure. It is relatively contraindicated during breastfeeding and in case of severe kidney failure. Its dosage regimen for children is 5 to 10 milligrams per kilogram per day, administered orally, and divided into 2 doses for 60 days. Its dosage regimen for adults is 5 milligrams per kilogram per day, administered orally, and divided into 2 doses for 60 days. It can cause allergic dermatitis, weight loss, anorexia, nausea, vomiting, abdominal discomfort, dose-dependent peripheral neuropathy, and leukopenia. The latter are enough reasons to stop treatment. Other adverse effects have been reported [19, 20].

7.1.2 Nifurtimox

It is absolutely contraindicated during pregnancy and in case of severe hepatic failure. It is relatively contraindicated during breastfeeding and in case of severe mental or psychiatric disorders, seizures, or kidney failure. Its dosage regimen for children is 10 to 15 milligrams per kilogram per day, administered orally, and divided into 3 doses for 60 days. Its dosage regimen for adults is 8 to 10 milligrams per kilogram per day, administered orally, and divided into 3 doses for 60 days. It can cause confusion, disorientation, insomnia, dizziness, headache, weight loss, anorexia, nausea, vomiting, abdominal discomfort, dose-dependent peripheral neuropathy or polyneuropathy, and leukopenia. The latter are enough reasons to stop treatment. Other adverse effects have been reported [19, 20].

Alternative dosage regimens can be consulted elsewhere, but their prescription should be aligned with country guidelines and policies. Biweekly reassessment of the complete blood count and hepatic and kidney tests is recommended [21, 22].

7.1.3 Emerging therapies

Antiarrhythmics (amiodarone/dronedarone), ergosterol inhibitors (albaconazole, fosravuconazole/ravuconazole, itraconazole, posaconazole, and voriconazole), nitroimidazoles (fexinidazole), purine synthesis inhibitors (allopurinol), and supplements (selenium) are being studied as emerging therapies [23].

7.2 Complimentary management

Once the cardiac and digestive forms have developed, they must be managed and treated: [14, 23].

7.2.1 Cardiovascular treatment

Infected individuals with the cardiac form of the disease must be encouraged to modify their diet and lifestyle. Pharmacological treatment (anticoagulants, antiarrhythmics, antihypertensives, β-blockers, cardiac glycosides, diuretics, and hypolipemiants) should be prescribed to decrease the cardiovascular risk, and surgical procedures (pacemaker

implantation, implantable cardiac defibrillators insertion, cardiac bridging, and heart transplantation) may be required to control or prevent complications [23, 24].

7.2.2 Gastrointestinal treatment

Infected individuals with the digestive form of the disease must be encouraged to modify their diet and lifestyle. Non-pharmacological treatment (pneumatic dilatation for megaesophagus and colon enemas for megacolon) and pharmacological treatment (botulinum toxin and sphincter relaxants for megaesophagus, and laxatives for megacolon) should be prescribed to decrease the duration and intensity of the clinical manifestations, and surgical procedures (cardiomyotomy and esophagectomy for megaesophagus, and anterior rectosigmoidoscopy, hemicolectomy, or total colectomy for megacolon) may be required to control or prevent complications [23, 25].

8. Prevention

8.1 Vector-borne transmission

Improving housing conditions, installing bed nets, and spraying insecticides indoors and outdoors can reduce the risk of acquiring Chagas disease through vector-borne transmission [5, 26].

8.2 Non-vector-borne transmission

Screening blood and organ donors and receptors can reduce the risk of acquiring Chagas disease through blood transfusions and organ transplantations. Screening women of childbearing age or who are pregnant can reduce the risk of acquiring it through congenital or vertical transmission. Strengthening hygienic measures while preparing and consuming beverages and food can reduce the risk of acquiring Chagas disease through oral transmission. Using standard precautions while handling and manipulating biological specimens can reduce the risk of acquiring it through accidental or occupational transmission [5, 26].

8.3 Prophylactic and therapeutic vaccines

Stopping Chagas disease transmission or progression can be done through vaccination. Primary prevention could be done with prophylactic vaccines, meanwhile, secondary prevention could be done with therapeutic vaccines. However, although several formulations and platforms have been tested in pre-clinical stages with encouraging and promising results, none is currently in clinical stages. The diversity of the parasite and the immunogenicity of the host are among the challenges that need to tackled. Investment is required to keep moving forward [27, 28].

9. Chagas disease and COVID-19

9.1 COVID-19

On December 31st, 2019, the WHO collected a media statement from the Wuhan Municipal Health Commission, in which they reported a cluster of atypical

pneumonia cases in Wuhan, People's Republic of China. On January 9th, 2020, Chinese investigators determined that the cluster of atypical pneumonia cases was caused by a novel coronavirus. On January 13th, 2020, the Ministry of Public Health of Thailand reported the first case outside of the People's Republic of China and on January 21st, 2020, the United States of America reported the first case in the American continent. The disease had quickly spread. On January 30th, 2020, the WHO declared that the novel coronavirus outbreak was a "Public Health Emergency of International Concern". On February 11th, 2020, the International Committee for Taxonomy of Virus named the virus "Severe Acute Respiratory Syndrome Coronavirus 2" (SARS-CoV-2), and the WHO named the disease "Coronavirus Disease 2019" (COVID-19). On March 11th, 2020, the WHO declared that COVID-19 could be characterized as a "pandemic" [29].

9.2 COVID-19 and NTDs

The COVID-19 pandemic has had a great impact on the economic and social spheres, disrupting essential health services and specific health programs worldwide. According to the WHO, 48 countries experienced disruptions in their NTDs programs, especially in low-and-middle-income countries in the African, American, Eastern Mediterranean, and South-Eastern Asian regions. Disruptions affected the community-based interventions (active case finding, awareness and education, hygiene and sanitation, mass treatment and preventive chemotherapy, psychosocial and rehabilitation services, vector control, and veterinary health), delayed health facility-based services (diagnosis and treatment, morbidity management, and disability prevention), interrupted the evaluation and monitorization of health programs (population surveys and routine surveillance), paused or slowed down the development, shipment, and transportation of consumables and medicines, and needed the reallocation of economic and human resources to support the COVID-19 response [30]. These increased the burden of most NTDs and jeopardized the fulfillment of the global targets for 2030 [31].

9.3 COVID-19 and Chagas disease

COVID-19 is a viral disease caused by the SARS-CoV-2 that has had a catastrophic global effect, [30] meanwhile Chagas disease is a parasitic disease caused by *T. cruzi* that has had a great impact in Latin America and that has become a global health issue [6]. Both are challenging and complex diseases with differences and similarities, which will be discussed from a practical perspective in this section of the book chapter:

9.3.1 Epidemiology

COVID-19 has been confirmed in about 768 million people worldwide, from which almost 200 million live in America, [32] where at least 6 million people have Chagas disease, and from which close to 1 million have developed the chronic determinate stage in its cardiac form. COVID-19 had a greater impact on this population, especially when essential health services were disrupted, and health systems were overloaded [33].

9.3.2 Etiology and transmission

COVID-19 is caused by a virus that belongs to the class *Pisoniviricetes*, order *Nidovirales*, family *Coronaviridae*, genus *Betacoronavirus*, and species *Severe acute*

respiratory syndrome-related coronavirus [8]. SARS-CoV-2 is a positive-stranded RNA virus that has been classified into clades, lineages, and variants, depending on the classification system. Each of them has their distribution and pathogenicity [34]. SARS-CoV-2 is primarily transmitted through aerosols and droplets exhaled by an infected individual, but contact transmission has also been reported [35]. COVID-19 and Chagas disease do not have common features in etiology and transmission, but SARS-CoV-2 has demonstrated that it evolves quickly and that it can be highly transmissive. This has been quite challenging for maintaining community-based interventions and health facility-based services that require face-to-face interactions during the pandemic. Chagas disease interventions and services were displaced [33].

9.3.3 Risk factors

Lack of awareness, living or visiting crowded or urban areas, being exposed to an infected individual, and having chronic diseases are the main risk factors for acquiring COVID-19 [36]. Besides the lack of awareness, COVID-19 and Chagas disease do not have common risk factors for acquiring them, but advanced age, cancer, chronic obstructive pulmonary disease, diabetes mellitus, hypertension, heart disease, and smoking are the main risk factors for developing severe COVID-19. Coinfected individuals do have a higher risk of developing severe COVID-19 because of aging and heart disease. On the other hand, the cytokine storm caused by COVID-19 can accelerate the progression of the chronic determinate stage, and immunodepression or immunosuppression are the main risk factors for having a reactivation of the disease. Coinfected individuals do have higher morbidity and mortality and have a higher risk of having a reactivation of the disease because of the overactivation of the immune system caused by COVID-19 and the administration of immunomodulators and steroids for its control [37].

9.3.4 Clinical manifestations

SARS-CoV-2 has an incubation period that ranges from 2 to 14 days. Infected individuals with COVID-19 can remain without clinical manifestations or can develop fever, anxiety, confusion, fatigue, weakness, dizziness, myalgia, arthralgia, headache, anosmia, dysosmia, rhinorrhea, dyspnea, cough, hemoptysis palpitations, chest pain, hyporexia, anorexia, nausea, vomiting, ageusia, dysgeusia, odynophagia, abdominal pain, diarrhea, and dermatosis [38]. *T. cruzi* has an incubation period that ranges from 7 to 14 days. Infected individuals with Chagas disease can remain without clinical manifestations or can develop fever, fatigue, weakness, myalgia, arthralgia, headache, nausea, vomiting, and abdominal pain during the acute stage of the disease; and, anxiety, confusion, fatigue, weakness, dizziness, dyspnea, cough, hemoptysis, palpitations, and chest pain, during the chronic stage of the disease in its cardiac form, or hyporexia, anorexia, nausea, vomiting, odynophagia, abdominal pain, and diarrhea during the chronic stage of the disease in its digestive form [14, 15]. COVID-19 and Chagas disease have a broad clinical spectrum that can overlap in some instances or stages. Coinfected individuals do develop arrhythmias, heart failure, and pulmonary thromboembolism with an increased frequency and severity. The background and clinical context are essential for intervening on time [33, 37].

9.3.5 Diagnosis

COVID-19 must be suspected when people that have been exposed to an infected individual experience the above-mentioned clinical manifestations, but it should be confirmed with laboratory tests. Detection of the antigens or the genetic material of SARS-CoV-2 in a nasal or nasopharyngeal swab can be done with an antigen test or with a PCR, respectively. Antigen tests are cheaper and quicker than PCR, but also are less sensitive and need to be repeated several times. Therefore, PCR is the gold standard for diagnosis. Detection of antibodies against SARS-CoV-2 in a blood sample can be done with serologic tests, but they are only useful for surveillance. In a couple of years, about 1000 brands of COVID-19 diagnostic tests became available for commercial use to test inside and outside hospital settings. Exposed individuals could go almost anywhere for testing [39]. In contrast, screening and testing for Chagas disease and other parasitic and tropical diseases were paused or slowed down, even in countries with plenty of resources. Exposed individuals had limited testing locations, and many did not go because they feared COVID-19 transmission. This situation has evidentiated the need for a better diagnosis framework and an expanded infrastructure to improve access and opportunity [40]. Furthermore, a complimentary examination is required for infected individuals who develop cardiac or digestive manifestations, but hospitals were overcrowded, and many patients were lost during their follow-up [37].

9.3.6 Treatment

COVID-19 can be treated with anti-inflammatories, antivirals, corticosteroids, interleukin-6 receptor blockers, and Janus kinase inhibitors, depending upon the severity of the disease [41]. Chagas disease can be treated with benznidazole or nifurtimox during the acute and chronic indeterminate stage [19, 20], and with anticoagulants, antiarrhythmics, antihypertensives, β-blockers, cardiac glycosides, diuretics, and hypolipemiants during the chronic determinate stage in its cardiac form [23, 24], or with botulinum toxin, sphincter relaxants, and laxatives during the chronic determinate stage in its digestive form [23, 25]. Coinfected individuals do need to treat both diseases, but doing it simultaneously can cause drug interactions and may increase the frequency and severity of adverse effects. Coinfected individuals must receive treatment for COVID-19 and Chagas disease during the acute stage or when there is reactivation, but should be delayed or postponed during the chronic indeterminate stage until COVID-19 is resolved. Drugs for the chronic determinate stage in its cardiac form should be screened and switched for controlling the disease and reducing the risk of complications, especially when azithromycin, chloroquine, hydroxychloroquine, and ivermectin have been administered for COVID-19 [33, 41], despite of the current evidence and recommendations [42].

9.3.7 Prevention

Avoiding crowds, keeping physical space, using face masks, and vaccinating can reduce the risk of acquiring COVID-19 through aerosols and droplets. Washing hands with soap and water can reduce the risk of acquiring COVID-19 through contact transmission. COVID-19 and Chagas disease do not have common features in prevention, but COVID-19 has demonstrated that adequate ventilation can reduce the risk of acquiring it, meanwhile, Chagas disease has demonstrated that adequate housing can

reduce the risk of acquiring it. Infrastructure is a common ground for both. Still, an effective and safe vaccine for Chagas disease is needed [41, 42].

10. Conclusions

Chagas disease has been historically neglected, but the efforts that have been made during the last decades have decreased its incidence in Latin America and have alerted the rest of the world about the mechanisms of its spread. However, the emergence of COVID-19 required the implementation of radical and unprecedented measures, including the reallocation of economic and human resources to control and mitigate the effects of an evolving and highly transmissible virus. Chagas disease became even more neglected. Exposed individuals could not be diagnosed and infected individuals could not be followed-up. Furthermore, coinfected individuals appeared in the scope. Chagas disease increases the risk of developing severe COVID-19, and COVID-19 enhances the progression or reactivation of Chagas disease. Up to date, we do not know much about its impact and pathophysiology. Research is required to better understand the consequences of its interaction.

The COVID-19 pandemic is far from over, but as we advance into the next stage of transition, we must acknowledge that what has been done during the last years should be applied to control, eliminate, and eradicate Chagas disease and other NTDs. Health professionals and policymakers must play their role and raise their voices to leave no one behind, especially those who are placed at the economic and social margins. We must develop a better framework to increase our infrastructure and overcome the challenges of our century in an improved and sustainable way.

Author details

Diego-Abelardo Álvarez-Hernández[1*], Daniella Pinto[2], Luis Martínez-Juárez[1], Rodolfo García-Rodríguez-Arana[2] and Alejandra Montoya[1]

1 Carlos Slim Foundation, Mexico City, Mexico

2 Universidad Anáhuac México, Mexico State, Mexico

*Address all correspondence to: dalvareh@fundacioncarlosslim.org

IntechOpen

References

[1] BMC Medicine. Putting chagas disease on the global health agenda. BMC Medicine. 2023;**21**(1):188. DOI: 10.1186/s12916-023-02885-9

[2] Álvarez-Hernández DA, Franyuti-Kelly GA, Díaz-López-Silva R, González-Chávez AM, González-Hermosillo-Cornejo D, Vázquez-López R. Chagas disease: Current perspectives on a forgotten disease. Revista Médica del Hospital General de México. 2018;**81**(3):154-164. DOI: 10.1016/j.hgmx.2016.09.010

[3] Martínez-Juárez LA, Álvarez-Hernandez DA, Sedas AC, Spencer J, Piot P. Defeating neglected tropical diseases in our new world living with COVID-19. Therapeutic Advances in Infectious Disease. 2020;**7**:1-3. DOI: 10.1177/2049936120971975

[4] Aborode AT, Fajemisin EA, Aiyenuro EA, Alakitan MT, Ariwoola MO, Imisioluwa JO, et al. Neglected tropical diseases (NTDs) and COVID-19 pandemic in Africa: Special focus on control strategies. Combinatorial Chemistry & High Throughput Screening. 2022;**25**(14):2387-2390. DOI: 10.2174/1386207325666220427123349

[5] World Health Organization. Chagas disease (also known as American trypanosomiasis). Available from: https://www.who.int/news-room/fact-sheets/detail/chagas-disease-(american-trypanosomiasis) [Accessed: August 2023]

[6] Lidani KCF, Andrade FA, Bavia L, Damasceno FS, Beltrame MH, Messias-Reason IJ, et al. Chagas disease: From discovery to a worldwide health problem. Frontiers in Public Health. 2019;**7**:1-13. DOI: 10.3389/fpubh.2019.00166

[7] Ortí-Lucas RM, Parada-Barba MC, de la Rubia-Ortí JE, Carrillo-Ruiz A, Beso-Delgado M, Boone AL. Impact of chagas disease in Bolivian immigrants living in Europe and the risk of stigmatization. Journal of Parasitology Research. 2014;**2014**:1-7. DOI: 10.1155/2014/514794

[8] Schoch CL, Ciufo S, Domrachev M, Hotton CL, Kannan S, Khovanskaya R, et al. NCBI Taxonomy: A comprehensive update on curation, resources, and tools. Database (Oxford). 2020;**2020**:baaa062. DOI: 10.1093/database/baaa062

[9] Rusman F, Floridia-Yapur N, Tomasini N, Diosque P. Guide RNA repertoires in the Main lineages of Trypanosoma cruzi: High diversity and variable redundancy among strains. Frontiers in Cellular and Infection Microbiology. 2021;**11**:1-14. DOI: 10.3389/fcimb.2021.663416

[10] Onyekwelu K. Life cycle of Trypanosoma cruzi in the invertebrate and the vertebrate hosts. In: De Souza W. Biology of Trypanosoma Cruzi. London, United Kingdom: IntechOpen; 2019. DOI: 10.5772/intechopen.84639

[11] Martín-Escolano J, Marín C, Rosales MJ, Tsaousis AD, Medina-Carmona E, Martín-Escolano R. An updated view of the Trypanosoma cruzi life cycle: Intervention points for an effective treatment. ACS Infectious Diseases. 2022;**8**(6):1107-1115. DOI: 10.1021/acsinfecdis.2c00123

[12] Coura JR. The main sceneries of Chagas disease transmission. The vectors, blood and oral

transmissions - A comprehensive review. Memórias do Instituto Oswaldo Cruz. 2015;**110**(3):277-282. DOI: 10.1590/0074-0276140362

[13] Daflon-Teixeira NF, Coutinho C, Gomes TF, Toma HK, Duarte R, Bóia MN, et al. Multiple approaches to address potential risk factors of chagas disease transmission in northeastern Brazil. The American Journal of Tropical Medicine and Hygiene. 2019;**100**(2):296-302. DOI: 10.4269/ajtmh.18-0480

[14] Álvarez-Hernández DA, García-Rodríguez-Arana R, Ortiz-Hernández A, Álvarez-Sánchez M, Wu M, Mejia R, et al. A systematic review of historical and current trends in chagas disease. Therapeutic Advances in Infectious Disease. 2021;**8**:1-17. DOI: 10.1177/20499361211033715

[15] Nunes MCP, Beaton A, Acquatella H, Bern C, Bolger AF, Echeverría LE. Et al; American Heart Association rheumatic fever, endocarditis, and Kawasaki disease Committee of the Council on cardiovascular disease in the young; council on cardiovascular and stroke nursing; and stroke council. Chagas cardiomyopathy: An update of current clinical knowledge and management: A scientific statement from the American Heart Association. Circulation. 2018;**138**(12):169-209. DOI: 10.1161/CIR.0000000000000599

[16] Balouz V, Agüero F, Buscaglia CA. Chagas disease diagnostic applications: Present knowledge and future steps. Advances in Parasitology. 2017;**97**:1-45. DOI: 10.1016/bs.apar.2016.10.001

[17] Pan American Health Organization, World Health Organization. Guidelines for the Diagnosis and Treatment of Chagas Disease. Washington, District of Columbia: PAHO; 2019

[18] García-Orozco VH, Villalvazo-Navarro JE, Solar-Aguirre C, Ibarra-Ocampo CM, Díaz-Sandoval CI, Ortíz-Gallegos CA, et al. Digestive disorders in chagas disease: Megaesophagus and Chagasic megacolon. In: Menna-Barreto R, editor. Chagas Disease. London, United Kingdom: IntechOpen; 2022. DOI: 10.5772/intechopen.102871

[19] Meymandi S, Hernandez S, Park S, Forsyth C. Treatment of chagas disease in the United States. Current Treatment Options in Infectious Diseases. 2018;**10**:373-388. DOI: 10.1007/s40506-018-0170-z

[20] Kawaguchi WH, Cerqueira LB, Fachi MM, Campos ML, Reason IJM, Pontarolo R. Efficacy and safety of chagas disease drug therapy and treatment perspectives. In: Nissapatorn V, oz HS. Chagas Disease - Basic Investigations and Challenges. London, United Kingdom: IntechOpen; 2018. DOI: 10.5772/intechopen.74845

[21] Dias JC, Ramos AN Jr, Gontijo ED, Luquetti A, Shikanai-Yasuda MA, Coura JR, et al. 2 nd Brazilian Consensus on Chagas Disease, 2015. Revista da Sociedade Brasileira de Medicina Tropical. 2016;**49**(1):3-60. DOI: 10.1590/0037-8682-0505-2016

[22] Médecins Sans Frontières. Clinical Guidelines - Diagnosis and Treatment Manual. Chapter 6. Parasitic Diseases. American Trypanosomiasis (Chagas Disease). Available from: https://medicalguidelines.msf.org/en/viewport/CG/english/american-trypanosomiasis-chagas-disease-63735484.html#section-target-3 [Accessed: August 2023]

[23] Álvarez-Hernández DA, Castro-Rico ZA, García-Rodríguez-Arana R, González-Chávez AM, González-ChávezMA,Martínez-JuárezLA, et al. Current treatment of chagas

disease. Current Treatment Options in Infectious Diseases. 2020;**12**:438-457. DOI: 10.1007//s40506-020-00238-1

[24] Cheng A, Slaughter MS. Heart transplantation. Journal of Thoracic Disease. 2014;**6**(8):1105-1109. DOI: 10.3978/j.issn.2072-1439.2014.07.37

[25] Pinazo MJ, Cañas E, Elizalde JI, García M, Gascón J, Gimeno F, et al. Diagnosis, management, and treatment of chronic chagas gastrointestinal disease in areas where Trypanosoma cruzi infection is not endemic. Gastroenterología y Hepatología. 2010;**33**(3):191-200. DOI: 10.1016/j.gastrohep.2009.07.009

[26] Liu Q, Zhou XN. Preventing the transmission of American trypanosomiasis and its spread into non-endemic countries. Infectious Diseases of Poverty. 2015;**4**:60. DOI: 10.1186/s40249-015-0092-7

[27] Dumonteil E, Herrera C. The case for the development of a chagas disease vaccine: Why? How? When? Tropical Medicine and Infectious Disease. 2021;**6**(1):16. DOI: 10.3390/tropicalmed6010016

[28] Maldonado E, Morales-Pison S, Urbina F, Solari A. Vaccine design against chagas disease focused on the use of nucleic acids. Vaccine. 2022;**10**(4):587. DOI: 10.3390/vaccines10040587

[29] World Health Organization. Timeline: WHO's COVID-19 Response. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/interactive-timeline#event-357 [Accessed: August 2023]

[30] World Health Organization. Control of Neglected Tropical Diseases. Available from: https://www.who.int/teams/control-of-neglected-tropical-diseases/overview/ntds-and-covid-19 [Accessed: August 2023]

[31] World Health Organization. Ending the Neglect to Attain the Sustainable Development Goals: A Road Map for Neglected Tropical Diseases 2021-2030. Geneva, Switzerland: WHO; 2020

[32] World Health Organization. WHO Coronavirus (COVID-19) Dashboard. Available from: https://covid19.who.int/ [Accessed: August 2023]

[33] Zaidel EJ, Forsyth CJ, Novick G, Marcus R, Ribeiro ALP, Pinazo MJ, et al. COVID-19: Implications for people with chagas disease. Global Heart. 2020;**15**(1):69. DOI: 10.5334/gh.891

[34] Centers for Disease Control and Prevention. COVID-19. Classifications & Definitions. Available from: https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html [Accessed: August 2023]

[35] Zhao X, Liu S, Yin Y, Zhang TT, Chen Q. Airborne transmission of COVID-19 virus in enclosed spaces: An overview of research methods. Indoor Air. 2022;**32**(6):1-14. DOI: 10.1111/ina.13056

[36] Shahbazi F, Solgi M, Khazaei S. Predisposing risk factors for COVID-19 infection: A case-control study. Caspian Journal of Internal Medicine. 2020;**11**(1):495-500. DOI: 10.22088/cjim.11.0.495

[37] Rodríguez-Morales AJ, Romani L, León-Figueroa DA. COVID-19 and chagas disease in Latin America. Revista del Cuerpo Médico Hospital Nacional Almanzor Aguinaga Asenjo. 2022;**15**(2):1-3. DOI: 10.35434/rcmhnaaa.2022.152.1499

[38] Da Rosa-Mesquita R, Francelino-Silva-Junior LC, Santos-Santana FM, Farias-de-Oliveira T, Campos-Alcántara R, Monteiro-Arnozo G, et al. Clinical manifestations of COVID-19 in the general population: Systematic review. Wiener Klinische Wochenschrift. 2021;**133**(7-8):377-382. DOI: 10.1007/s00508-020-01760-4

[39] Peeling RW, Heymman DL, Teo YY, Garcia PJ. Diagnostics for COVID-19: Moving from pandemic response to control. Lancet. 2022;**299**:1-12. DOI: 10.1016/S0140-6736(21)02346-1

[40] Green A. Calls to restart testing for parasitic disease at US CDC. Lancet. 2022;**399**(10338):1855. DOI: 10.1016/S0140-6736(22)00872-8

[41] Diaz-Hernandez A, Gonzalez-Vazquez MC, Arce-Fonseca M, Rodriguez-Morales O, Cedilllo-Ramirez ML, Carabarin-Lima A. Risk of COVID-19 in chagas disease patients: What happen with cardiac affectations? Biology (Basel). 2021;**10**(5):1-15. DOI: 10.3390/biology10050411

[42] World Health Organization. Therapeutics and COVID-19: Living Guideline. Available from: https://app.magicapp.org/#/guideline/6914 [Accessed: August 2023]

Chapter 4

Neglected Diseases in Brazil: Space-Temporal Trends and Public Policies

Nádia Teresinha Schröder, Eliane Fraga Da Silveira, Letícia Thomasi Janhke Botton and Eduardo Périco

Abstract

In the twenty-first century, neglected tropical diseases still remain a serious public health problem, especially in developing countries. Meeting several sustainable development objectives of the 2030 Agenda, by countries that are in this condition, will provide the population with another level of quality of life. In Brazil, this situation is far from being resolved, since its dimensions are continental, there is a lot of social inequity, lack of basic services, health, and education. In this context, the scenario of the last 10 years of six neglected tropical diseases that are classified as notifiable in Brazilian territory is presented. There are several public policies established by the Federal government containing actions, strategies, and programs to try to reduce the burden of these diseases, but there is a lack of political will for states and municipalities to comply with the established in order to achieve all objectives and goals. It is still necessary to have an active participation of the population so that the reduction process can be started for possible elimination.

Keywords: public health, developing countries, compulsory notification, Brazilian territory, health strategies

1. Introduction

Neglected tropical diseases (NTDs) form a group of diseases caused by infectious agents or parasites and are considered endemic, occurring mainly among low-income and marginalized populations in tropical and subtropical regions of the world, mainly in Africa, Asia, and Latin America. These diseases disable or lead to the death of millions of people and represent an important medical need that remains unmet [1]. There are 20 groups of NTDs, of which 14 occur in Brazil, which lead, along with three other African countries, to the global distribution of these diseases [2, 3].

Brazil is the largest country in South America and is located between the parallels of 5° 16′20" North and 33° 45′03" South and the meridians of 34° 47′30″ and 73° 59′32" West. It is the fifth largest country in the world in land area with an extension of 8,515,767.049 km^2. The country is cut by the Equator and Tropic of Capricorn, with

most of its territory located in the lowest latitudes of the globe, which gives it characteristics of a tropical country [4].

The Brazilian geographical extension and diversity allow for a wide variety of climates. The main climate zones in the country are: Equatorial climate (Amazon region); Tropical climate (most of Brazil, especially in the central and coastal regions); Semi-arid climate (predominantly northeast Brazil); Subtropical climate (south of the country).

Brazil is considered a country susceptible to climate change due to deforestation, forest fires, loss of biodiversity, air and water pollution, disorderly urbanization, and impacts on coastal communities due to rising sea levels. In addition, Brazil faces challenges regarding the implementation of policies to mitigate and adapt to climate change. The Amazon and the Cerrado play an important role in regulating the global climate and maintaining biodiversity [4]. Regarding the diversity of fauna and flora, it is one of the most biodiverse countries in the world, home to a wide variety of ecosystems and species. Considered one of the largest tropical forests on the planet, the Amazon Rainforest is known for its great biological diversity. In addition, the Brazilian territory has other biomes such as the Cerrado, the Atlantic Forest, the Caatinga, the Pantanal, and the Pampas region. However, deforestation, urbanization, unsustainable exploitation of natural resources, pollution, and climate change are conditions that have altered Brazilian biodiversity. The conservation of these ecosystems and species is an important concern to guarantee the sustainability, the environmental balance in the country and to help in adequate environmental conditions to prevent the transmissibility of diseases [4].

In Brazil, there is a concentration of neglected diseases, and the implementation of public policies has been carried out in order to promote protection to the citizens. In this context, fundamental, human, and social rights and their respective guarantees, protections, and individual and collective rights are contemplated in the Constitution of the Federal Republic of Brazil [5]. Among its fundamental principles is that of human dignity, which is an autonomous normative force, with a multidimensional character [6]. In a logical-juridical-social analysis, social rights must have a solid relationship between the resources used and the effective capacity to achieve efficient results. These rights are materially made available to the Brazilian population, based on public policies, which are instruments that are used to safeguard the principle of human dignity [7]. One of the public health problems in Brazil is NTDs. The expansion of cases of these injuries is linked to the precariousness of other rights, subjectively guaranteed by the FC, such as basic sanitation, access to drinking water, and health services in an integral and universal way [8].

NTDs are diseases that receive little attention from the government and have less incentives in terms of research and investment in health, production of new drugs, training of professionals for early and correct diagnosis, adequate socio-environmental infrastructure, health education, and monitoring and vector control [1]. However, the signatory countries of the 2030 Agenda are committed to achieving the sustainable development goals, elaborated interdependently, and aimed at stimulating actions that meet human needs, access to rights, and basic services [9]. The reduction of epidemics caused by NTDs is among the goals of meeting the Sustainable Development Goals, whose disease prevention, expansion, and consolidation of vaccine coverage and access to correct treatment are priorities [10].

The control of NTDs involves actions aimed at involving public authorities, the local population, health professionals, and operational technicians who participate

in the monitoring and reporting of diseases. This is necessary to obtain intersectoral work with broad engagement with the challenge of prevention and control and intervention in specific scenarios [10]. These efforts are essential for a strategic and coordinated response by developing countries to deal with the growing burden and threat of these diseases, especially in times of epidemic outbreaks. A common approach to the elimination of NTDs becomes paramount, as there are tools and technologies that make it feasible. It is necessary to promote integration and synergy between priority public health programs and primary health care centered on the local and regional community and on the health provisions offered to all [10].

Among the main NTDs are malaria, dengue, Chagas disease, leishmaniasis, and schistosomiasis, whose transmission patterns are influenced by socioeconomic, demographic, and environmental factors. These diseases impede economic development due to their direct and indirect costs, such as loss of productivity, for example. Unplanned urbanization, increased movement of people, environmental changes, and biological challenges, such as insecticide-resistant vectors, increase the risk of transmission, and allow the population to be exposed to emergency risk [11].

Health systems must be prepared to detect and respond to epidemiological changes in these diseases quickly and efficiently. This response requires not only the availability of effective and evidence-based control interventions but also health professionals and staff trained for this demand [11]. Most of these can be avoided based on a properly implemented control and prevention that optimizes programs and interventions aligned with the local and regional context, monitoring system, and population participation.

Brazil does not have specific legislation establishing a public policy whose main objective is the elimination and/or reduction of NTDs, but there are specific infraconstitutional laws that address them. Several strategies have been adopted and among the main public policies are:

1. Neglected Tropical Diseases Control Program: prioritizes the prevention and control of diseases such as Chagas disease, leishmaniasis, schistosomiasis, among others. It involves diagnosis, treatment, epidemiological surveillance, training of health professionals, and social mobilization.

2. Distribution of medicines: guarantee of free access to medicines for the treatment of NTDs distributed in health units.

3. Research and development: investment in scientific research for the development of new tests for diagnosis, drugs, and prevention.

4. Strengthening epidemiological surveillance: monitoring the occurrence and geographic distribution of NTDs in order to identify cases, investigate outbreaks, and implement control measures.

Despite the efforts of the Brazilian government, there are still challenges to be faced. The lack of adequate infrastructure in some regions, the difficulty of accessing remote areas, socioeconomic inequality, and lack of awareness among the population are obstacles to the effective control of NTDs. Continuous work is needed, involving integrated actions between different sectors of society, to reduce the incidence and improve the quality of life of the affected populations.

2. Outline and study area

From an ecological, descriptive, and retrospective analysis, having NTD notifications as a universe, from 2012 to 2022, it was possible to establish the spatial and temporal scenario of six neglected tropical diseases (dengue, visceral leishmaniasis, malaria, schistosomiasis, Chagas disease, and leprosy) that affect the Brazilian population. For this, we used data obtained from the Unified Health System, DATASUS, in the public domain. (https://datasus.saude.gov.br/acesso-a-informacao/doencas-e-agravos-de-notificacao-de-2007-em-diante-sinan/). This system uses the files of the Notifiable Diseases Information System (SINAN) as a source, which enables the global and integrated analysis of information related to priority diseases in Brazil. Data from the local base is transferred between the different levels of management of the system, being distributed to the coordinators of each condition.

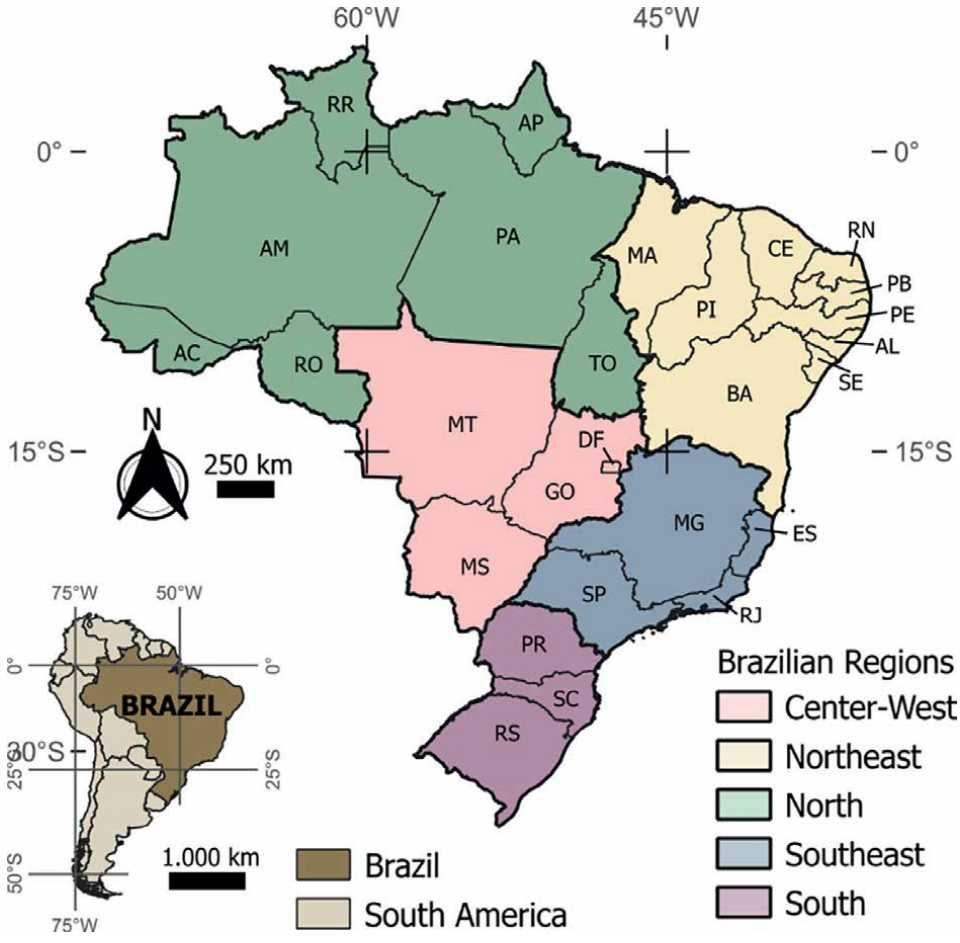

Figure 1.
Brazil is geographically divided into five macro-regions. Center-West (DF: Distrito Federal, GO: Goiás, MT: Mato Grosso and MS: Mato Grosso do Sul); North (AC: Acre, AM: Amazonas, AP: Amapá´, RO: Rondônia and RR: Roraima); Northeast (AL: Alagoas, BA: Bahia, CE: Ceara´, MA: Maranhão, PB: Paraíba, PE: Pernambuco, PI: Piauí, RN: Rio Grande do Norte and SE: Sergipe); South (PR: Paraná, RS: Rio Grande do Sul and SC: Santa Catarina); Southeast (ES: Espírito Santo, MG: Minas Gerais, RJ: Rio de Janeiro and SP: São Paulo).

NTD incidence rates were calculated by sex and region, using the equation: number of notifications for NTDs divided by the total population size of the region ×100,000. Population data are in line with the 2022 census [12]. The maps were prepared in QGIS software, version 3.28.2 using the cartographic base of the Brazilian territory (state boundaries) provided by IBGE. After elaboration, they were edited in CorelDraw for better finishing. (https://www.ibge.gov.br/geociencias/organizacao-do-territorio/malhas-territoriais/15774-malhas.html).

The SINAN and IBGE databases, which are in the public domain, do not allow the identification of individuals. In this context, this study is based on Resolution No. 510/2016 of the National Health Council (CONEP), which establishes the non-mandatory analysis of ethics in studies that use secondary data and that are publicly available and do not provide information that identifies individuals (http://conselho.saude.gov.br/resolucoes/2016/reso510.pdf).

Brazil is the largest country in Latin America, with a population of around 214 million inhabitants and a density of 23.86 inhabitants/km^2, in a territorial area of 8,510,417.771 km^2 [12] (https://cidades.ibge.gov.br/brasil/panorama). The country borders nine countries in South America: Uruguay, Argentina, Paraguay, Bolivia, Peru, Colombia, Venezuela, Guyana, and Suriname, in addition to the French Overseas Department of Guyana. Politically and administratively, Brazil is divided into 26 states and a Federal District. The Federation is made up of five macro-regions (North, Northeast, Southeast, South and Midwest) and 558 micro-regions containing 5570 municipalities with different environmental and cultural characteristics (**Figure 1**).

3. Space-time analysis of the main NTDs in Brazilian territory

According to data obtained from SINAN, between 2012 and 2020, a total of 10,455,616 individuals with an NTD were reported in the Brazilian territory. Among the diseases analyzed, dengue and leprosy had the highest number of reported cases (**Table 1**).

Considering the NTDs among the regions of Brazil, dengue was the most notified in all regions of the country. The percentage of infected ranged from 80.7% in the North region to 98.1% in the South region. Chagas disease had the highest occurrence in the North region, although the frequency in the other regions was below 0.004%. Leprosy (17.4%) and visceral leishmaniasis (1.2%) were more frequent in the Northeast region. Malaria had a low frequency in all regions, and the absence of cases in the North is an indication of underreporting. Schistosomiasis was more prevalent in the Southeast (0.70%) and Northeast (0.51%) regions. The concentration of NTDs was higher in the Southeast region, with 53.7% of notifications, due to dengue notifications (5,498,518 cases) (**Figure 2**).

The profile of those affected, when considering the gender of the individuals, made it possible to identify that men are more prevalent in all NTDs, with the exception of dengue (**Figure 3**).

From the calculated incidence rates for NTDs, by sex, in the different regions, it was observed that malaria affected men more (0.3–1.0/100,000 inhabitants.) in the Midwest region when compared to other regions. Visceral leishmaniasis had a higher incidence rate in men in all regions, but the Northeast (4.4/100,000 inhabitants.) and North (3.7/100,000 inhabitants) regions had the highest rates. Schistosomiasis occurred mainly in the Northeast and Southeast regions, with a higher incidence in males. Dengue is the disease with the highest incidence in all regions of the country,

Macroregions	Malaria	Visceral leishmaniasis	Schistosomiasis	Dengue	Chagas disease	Leprosy	Total
North	0	5981	613	404,666	2681	87,258	501,199
Northeast	1273	19,416	11,349	2,018,979	100	192,054	2,243,171
Southeast	3228	6481	39,127	5,498,518	12	68,001	5,615,367
South	899	122	524	933,383	4	15,998	950,930
Center-West	1052	2854	632	1,984,431	12	89,351	2,078,332
Total	6452	34,854	52,245	9,906,594	2809	452,662	10,455,616

Table 1.
Number of people infected with neglected diseases by region in Brazil, between 2012 and 2022. (Source: SINAN, 2023).

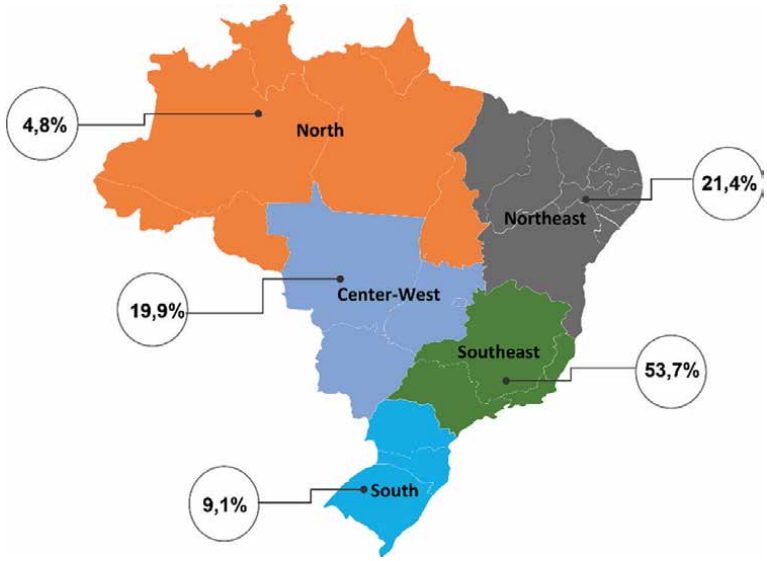

Figure 2.
Percentage of NTDs between regions of Brazil in the period from 2012 to 2022.

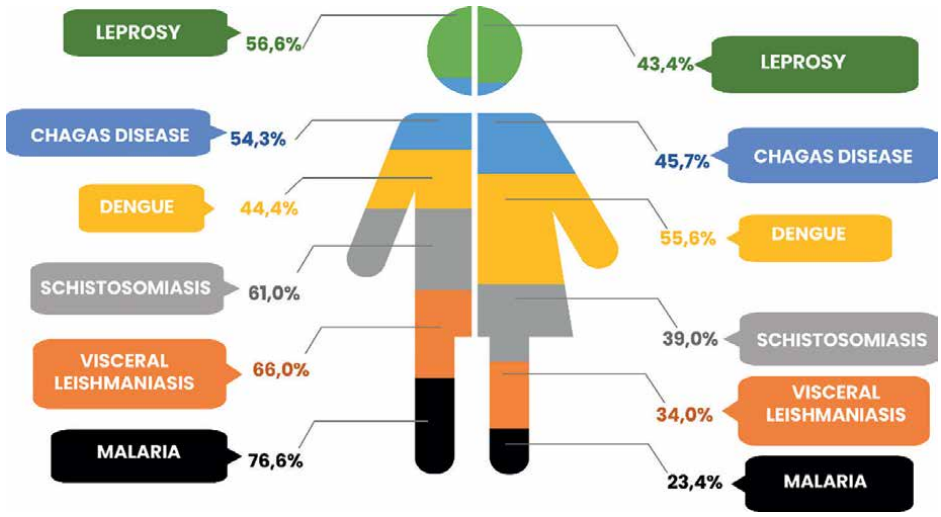

Figure 3.
Percentage of those infected notified by NTD group and sex, in the period 2012 and 2022, in Brazil.

with greater prominence in the Midwest region with a rate of 1238.7/100,000 inhabitants in women. Females had higher incidence rates in all regions. Chagas disease had the highest number of records in the Midwest region, with a predominant incidence in males. Leprosy had the highest incidence rates in males in the Midwest and North regions (**Figure 4**).

Among the forms of transmission of the diseases studied, four have vector transmission (dengue, visceral leishmaniasis, malaria, and Chagas disease) (**Figure 5**). Dengue was the NTD with the highest percentage in all regions, and transmission occurs through the bite of females of the *Aedes aegypti* species, popularly known as

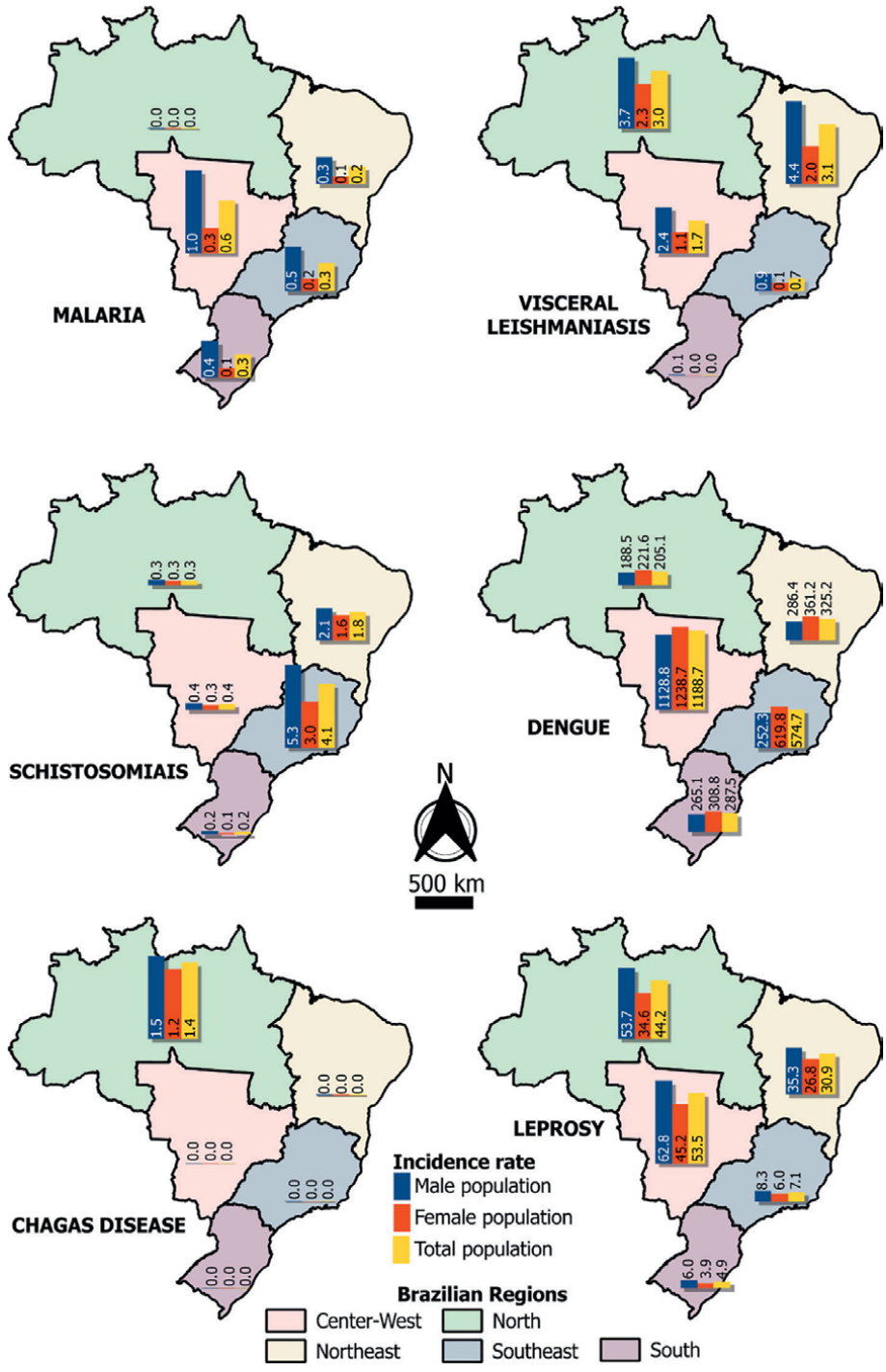

Figure 4.
Incidence rate of neglected tropical diseases (NTD) in the regions of Brazil, between 2012 and 2022.

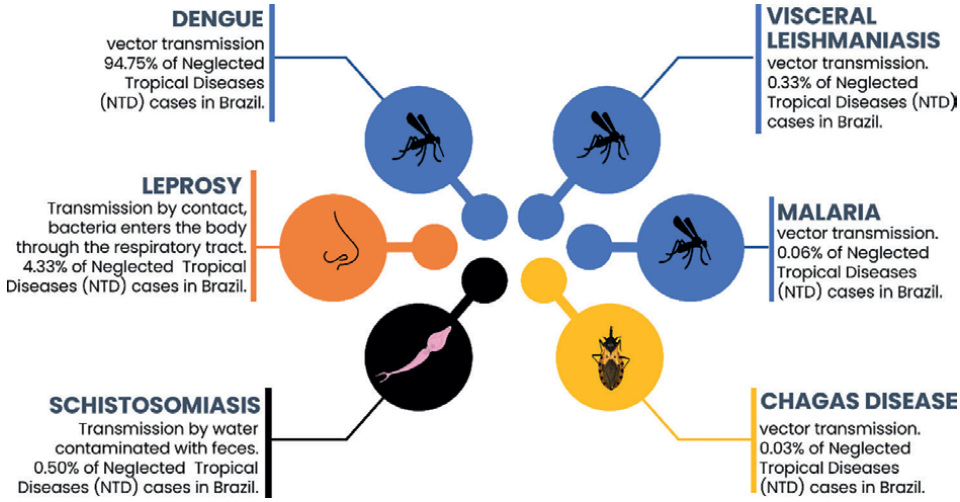

Figure 5.
Neglected tropical diseases (NTD), mode of transmission, and percentage of notifications in Brazil, between 2012 and 2022.

the dengue mosquito or black stilt. This vector is from the Culicidae family, with a wide distribution in the country and anthropophilic habits (depending on the human presence in the place to establish itself). The *A. aegypti* species is well adapted to urban areas, mainly in human homes [13]. Leprosy had the second highest prevalence among NTDs, and is a disease transmitted by continuous contact with infected people [14]. Schistosomiasis is a disease that is directly related to risk areas that have unfavorable sanitary conditions. The infective larvae are in bodies of water contaminated with human feces from carriers of *Schistosoma mansoni* which causes water belly or human *schistosomiasis* [15].

4. Brazilian public policies for main NTDs

Brazil has specific federal public policies established for the control of NTDs and implemented in states and municipalities. These policies aim to prevent the transmission of disease, reduce the incidence of cases, and improve the quality of life of the population. It is important to emphasize that the strategies (**Figure 6**) used by the Brazilian government may vary according to the region and the epidemiological situation of each location [16, 17].

The surveillance system is responsible for monitoring the occurrence of cases throughout the country, identifying areas of risk, prevalence, incidence, outbreaks, and adopting preventive and control actions. This involves data collection, analysis, and sharing of relevant information to guide strategies to combat these diseases [18]. The Notifiable Diseases Information System (SINAN) is a platform of the federal government for the dissemination of notified data in the national territory [16].

The government promotes health awareness and education campaigns, aiming to inform the population about the risks, prophylactic measures, prevention, and

Figure 6.
Government actions for six NTDs in Brazilian territory.

recognition of signs and symptoms. These campaigns are carried out through the media (radio, television, and internet), in addition to the distribution of educational materials and other social mobilization actions encouraging active participation in environmental care and the adoption of appropriate hygienic practices [19].

Vector control is one of the main strategies adopted. Actions include the elimination of breeding sites, larvicide and insecticide spraying actions, use of mosquito nets impregnated with insecticide, residential screens, and health education [11, 16].

The training of health professionals, both in the public and private networks, is an important strategy for early diagnosis and adequate treatment of cases. This includes training physicians, nurses, and other professionals in the field on clinical management protocols for these diseases [20].

The Brazilian Ministry of Health has implemented screening programs in blood banks, public agencies, and other strategic locations, with the aim of identifying infected individuals [21], performing early diagnosis, and offering adequate and free treatment [2]. Access to treatment is one of the main concerns of public policies.

Environmental management aims to reduce the number of sites conducive to the development of vectors/hosts. In addition, improving basic sanitation conditions is an important strategy for controlling NTDs. This reduces the exposure of the population to the risk of contamination [19].

Comprehensive care for patients with these diseases is necessary. This includes regular clinical follow-up, psychosocial support, rehabilitation, and disability prevention, as well as actions to promote social inclusion. In addition, the Ministry of Health provides medication free of charge, with the aim of reducing the progression of diseases and improving the quality of life of patients [20, 22].

Within the strategies designed for the monitoring and prevention of NTDs, the Federal Government has established some national programs:

1. National Dengue Control Program *(Programa Nacional de Controle da Dengue* - PNCD*)*: prioritizes the reduction of infestation by *Aedes aegypti*; incidence and

lethality due to dengue hemorrhagic fever. For this, it emphasizes some essential aspects such as: the elaboration of permanent programs; the development of information and mobilization campaigns; strengthening epidemiological and entomological surveillance; improving the quality of vector combat field work; the integration of dengue control actions in primary care, with the mobilization of the Community Health Agents Program (Pacs) and the Family Health Program (PSF) *Programa Saúde da Família*; the use of legal instruments that facilitate the work of public authorities; multisectoral action and the development of more effective instruments for monitoring and supervising the actions developed by the Ministry of Health, states, and municipalities [23].

2. Schistosomiasis Control Program (*Programa de Controle da Esquistossomose* - PCE*)*: it was proposed with the aim of eliminating schistosomiasis as a public health problem. It provides morbidity control using early diagnosis, classification of risk areas, and treatment strategies for those affected in endemic areas. It also carries out health education activities and mobilization of communities at risk. In the environment, it performs the mapping of water collections, control of snails, and interventions in outbreaks of transmission with chemical control when indicated. They propose an interface and articulation with environmental agencies responsible for domestic and environmental sanitary conditions. In addition, it seeks to observe the scenario in endemic and non-endemic areas through the notifications of cases in SINAN [22].

3. National Leprosy Control Program (*Programa Nacional de Controle da Hanseníase* - PNCH): It aims to reduce the incidence of the disease, diagnose early, and provide adequate treatment. The program promotes epidemiological surveillance actions, training of health professionals, health education, multidisciplinary treatment, and social reintegration of patients [24].

4. National Leishmaniasis Surveillance and Control Program (*Programa Nacional de Vigilância e Controle da Leishmaniose* - PNVCL): It aims to control the transmission of leishmaniasis and reduce its morbidity and mortality. The program encourages epidemiological surveillance actions, early diagnosis, adequate treatment, vector control, and health education and canine vaccination actions in endemic areas [25].

5. National Malaria Control Program (*Programa Nacional de Controle da Malária* - PNCM): It aims to reduce morbidity and mortality caused by the disease, based on actions such as diagnosis, treatment, epidemiological surveillance, training of health professionals, and prevention actions [26].

5. Social determinants of DTNs

NTDs affect the poorest and most disadvantaged people in tropical and subtropical regions of the world. The injuries can cause suffering and permanent disability of men, women, and children, resulting in generations condemned to illness and misery [27]. The scenario is challenging and requires an irrevocable commitment from countries to control NTDs and improve quality of life.

In Latin America, Brazil is the leader in the number of cases of Chagas disease, leishmaniasis, leprosy, dengue, and schistosomiasis, which is why they are classified as priorities by the Ministry of Health. The epidemiological picture shows the vulnerability of epidemic occurrences, the risk of increasing deaths and lethality [17].

In relation to priority health problems in Brazil:

1. **Dengue**: It is the most prevalent urban arbovirus in the Americas, and is an acute febrile viral disease, with seasonal, systemic, and dynamic characteristics, presenting a broad clinical spectrum, ranging from asymptomatic to severe cases. It occurs in environments with climatic and environmental conditions favorable to the development and proliferation of vectors (*Aedes aegypti*). Common characteristics of tropical and subtropical countries present local risk variations influenced by precipitation, temperature, and unplanned urbanization [23, 28]. This disease has epidemiological patterns, hyperendemicity of several serotypes of the virus, in addition to affecting the health of the population and the economies of countries that are unable to minimize or eliminate the disease. With this scenario, it has been observed that the burden on health services and their cost to countries has increased. The maintenance of the disease causes outpatient and hospital expenses, in addition to surveillance activities, vector control and population mobilization. The incidence of dengue has increased a lot all over the world, but the real number of cases of the disease is underreported and many are misclassified. Thus, the global burden of the disease remains uncertain [28]. Furthermore, early detection and access to adequate health services reduce mortality rates to below 1% [28]. The great challenge of the epidemiological scenario of dengue in Brazil, characterized by the simultaneous circulation of the four virus serotypes, is the work of assistance and surveillance. Urban arboviruses are similar in that they share several clinical signs. This has made it difficult for health professionals to adopt appropriate clinical management, which can progress to severe forms and eventual death [17].

2. **Chagas disease**: It is also known as American trypanosomiasis. It is a parasitic disease caused by the protist *Trypanosoma cruzi*, which is transmitted by an insect vector (kissing bug), blood transfusion, organ transplantation, consumption of contaminated food, or during pregnancy [29]. It is part of the NTD group, endemic in Latin America and has a high prevalence and morbidity and mortality burden, thus maintaining a critical cycle of vulnerability and representing one of the four major causes of death from infectious and parasitic diseases [30]. In 2020, chronic Chagas disease was defined as a nationally notifiable disease [31]. In this context, the need for an adequate social response is evident, based on the efforts of public authorities and health networks (Health Care Network – RAS *Rede de Atenção à Saúde* and the Unified Health System – *Sistema Único de Saúde* SUS) [32], in addition to the community participation in environmental care.
   The prevention of Chagas disease is closely related to the form of transmission. The control of the disease must be through the elimination of the vector and quick access to health services for infected people. Vector control has been the most effective method of preventing and controlling the disease in Latin America and has a lower cost when compared to the amount spent on medical care for patients with cardiac, digestive, neurological, or mixed forms of the disease [33]. The determinants and conditions that contribute to the transmission

of trypanosomatid are uncontrolled human migration, unplanned urbanization with population concentration and socio-environmental and economic vulnerability. These conditions generate inequalities that, for infected populations, result in greater risk [34]. Consequently, there is low quality in the Primary Health Care (PHC) services provided, difficulty in diagnosing, not guaranteeing the integration of patient care, and failures in preventive interventions. In this context, there is a probability of an increase in the development of severe forms of the disease. The lack of knowledge of health professionals and managers and the population about the risk conditions and identification of new cases, late diagnosis, and inopportune treatment help in the disease chronicity which causes significant sequelae, which may progress to death [33]. Knowing how to recognize the weaknesses of the Brazilian health system is necessary for greater control of the disease and the identification of epidemiological scenarios. This knowledge is essential for the effective success of effective and efficient management, surveillance, control, and health care strategies and actions [35]. The territorialization of both information and professional performance can be allies in improving public health. The demarcation of areas of activity in the Health Units, in addition to the integration of actions and practices of integral reception of the care for the carrier of Chagas disease, is necessary [34].

3. **Schistosomiasis**: It is an endemic parasitosis caused by *Schistosoma mansoni* that occurs in Brazilian territory with an important health impact on the affected populations in Brazil and worldwide. The conditions that contribute to the occurrence of the injury are places without sanitation or with inadequate basic sanitation, socioeconomic conditions, occupation, leisure, education, and population exposure to risk. The prevalence of parasitosis is also linked to the growth of urban centers, which leads to the establishment of human settlements in peripheral areas, lacking minimal sanitary infrastructure. This scenario creates conditions for the maintenance and transmission of the injury [36, 37]. The complex transmission mechanism of schistosomiasis, together with the different conditions for the cycle to occur, means that the control of the disease requires preventive actions such as: early diagnosis and adequate treatment; monitoring of environmental conditions favorable to transmission, the establishment of adequate basic sanitation and health education [36]. In this context, it is up to the municipalities and especially to the managers of both the Unified Health System and the other government sectors involved in environmental intervention and education actions to articulate themselves so that there is an effective and efficient control of schistosomiasis, in addition to carrying out, in an organized and regular manner, the active search for carriers and promoting timely treatment, in order to maintain low prevalence and reduce severe forms [37]. This work is necessary to contain the geographic expansion of schistosomiasis and the advance of the silent infection [36].

4. **Leprosy**: It is an infectious disease caused by the bacteria *Mycobacterium leprae* (Hansen's bacillus) and transmitted by close and frequent contact with untreated infected people [38]. The disease can cause progressive and permanent sequelae, such as deformities and mutilations, reduced limb mobility and even blindness, when not treated at the onset of signs and symptoms [39].
   In the Americas, Brazil has the highest burden of leprosy and the second highest in the world, being a public health problem. It is a treatable disease, which is

curable, and early diagnosis and treatment are essential to avoid complications and reduce the chances of the affected person having a disability, and prevent transmission. Leprosy treatment is free [38].

The disease is associated with stigma, especially when deformities are present. This situation has a negative impact on access to diagnosis, on the outcome of treatment and care, in addition to violating civil, political, and social rights. Ending discrimination, stigma, and prejudice is essential for eliminating leprosy [38–40]. In order to minimize this problem, the Principles and Guidelines for the elimination of discrimination against people affected by leprosy and their families were established worldwide. These principles and guidelines make national governments responsible for eliminating discrimination related to it. Most endemic countries have made efforts to integrate leprosy care services into their health services [38, 40]. An important legislative and social landmark of leprosy was Ordinance No. 165/95, which established the Leprosy Control Policy prohibiting the terms "leprosy", "leper" and derivatives [41]. The National Strategy for Combating Leprosy 2019–2022 seeks to guide services at all levels, considering the complexity of cases, in compliance with the principles of the Unified Health System, strengthening actions related to leprosy with the aim of promoting the promotion of health [33, 42]. To enhance these actions and strategies, the month of January was designated as the month of alert for leprosy and the color purple was defined. Brazil became the first country in the world to offer inputs in the public network for the detection of the disease, from the distribution of rapid tests to support the diagnosis of leprosy in the SUS [43].

5. **Leishmaniasis**: It is an infectious disease caused by parasites of the genus *Leishmania*, transmitted by the bite of sandflies, also known as sandflies or birigui. There are three main forms of leishmaniasis: visceral, cutaneous, and mucocutaneous [25]. This condition continues to be an important health problem in four eco-epidemiological regions of the world: Americas, East Africa, North Africa, West and Southeast Asia. It is among the top 10 NTDs, being endemic in 99 countries and its occurrence is directly related to poverty, social, environmental, and climatic factors, which directly influence its epidemiology [44].

   In the Americas, leishmaniasis is zoonoses with notification of 85% of cases in three countries (Brazil, Colombia, and Peru). There is a situation that makes clinical and therapeutic management difficult and becomes more costly, which is Leishmania-HIV co-infection, already registered in 42 countries [44].

   In Brazil, visceral leishmaniasis, also called kala-azar, is the most common (68%) and severe form of the disease and can be fatal if not properly treated. It is endemic in the North, Northeast, and Midwest regions [25, 44], but with cases registered in other parts of the nation. The profile change in the manifestation of visceral leishmaniasis was evidenced in all regions of the country by the predominance of its occurrence in urban areas [45].

   Exposed persons should take measures to reduce contact with the vector and avoid exposure to areas with a high incidence of the disease [25, 46]. Euthanasia of the reservoir is not advised, as the dog is not responsible for transmitting the disease [45, 47]. Contributing to this, the Ministry of Health established, as a control tool for canine visceral leishmaniasis in the most affected municipalities, the distribution of collars impregnated with insecticide. In some regions of the country, testing on dogs has been adopted as another way to maintain monitoring [48]. In addition, health authorities must implement surveillance

actions and, when necessary, carry out public health interventions, considering the standardized risk stratification for leishmaniasis. Early diagnosis is essential to establish adequate treatment, prevent disease progression, relieve signs and symptoms, reduce mortality, and improve patients' quality of life [44].

It is important to emphasize that the control of leishmaniasis is complex due to the wide geographic distribution of the disease in a country with continental extensions. In addition, community participation and the integration of different sectors, such as health, environment, and agriculture, are essential for the success of public policies to control this disease [25]. In this context, Brazil performs risk stratification of municipalities with transmission based on the classification used by the Pan American Health Organization (PAHO). This stratification aims to direct and prioritize the planning, execution, and evaluation of municipal surveillance, prevention, and control actions in defined territories. The municipalities are stratified according to the transmission intensity (low, medium, high, intense, and very intense) [46].

6. **Malaria**: It is an infectious disease transmitted by the bite of the genus *Anopheles* mosquito infected with the *Plasmodium* parasite and presents a risk of death but can be prevented and cured. *Plasmodium vivax* and *P. falciparum* are the most common parasite species found in Brazil. *P. vivax* is the most prevalent and usually causes a milder form of the disease, while *P. falciparum* is responsible for the most severe and potentially fatal form of malaria [49, 50].

   There is a risk of malaria in 18 countries, but the WHO certified Paraguay, Argentina, and El Salvador as malaria-free regions in 2018, 2019, and 2021, respectively [50]. In Brazil, malaria is considered a public health problem, although its impact has decreased significantly in recent decades. Its distribution is uneven, with a higher incidence in the Amazon region. The states of the Legal Amazon, such as Amazonas, Pará, Rondônia, and Acre, have the highest rates of cases. However, other states, such as Maranhão, Mato Grosso, and Tocantins, also register cases of the disease [49].

   Malaria prevention involves several environmental strategies, early diagnosis, and adequate treatment of cases [51]. Over the years, Brazil created services, departments, and institutes that developed plans, actions, programs, and measures to interrupt the transmission of malaria [52]. As in 2000, when the Brazilian government established strategies to combat malaria such as creating: the Plan for Intensifying Malaria Control in the Legal Amazon, the Health Surveillance Secretariat and the National Malaria Control Program, the Epidemiological Surveillance Information System (Sivep-Malaria), the participation in the Global Fund Project, the Plan to Eliminate Falciparum Malaria and the observance of the Sustainable Development Goals. Actions include: broad coverage of free diagnoses and treatments; online computerized system; partnerships in various sectors and malaria research network. There are still challenges such as ensuring access of patients with this disease to the primary care, early diagnosis, and timely and adequate treatment in remote areas, updating professionals, special attention to indigenous and mining areas, and environmental surveillance aimed at elimination of the vector [52].

   The reality of the epidemiological situation shows a decrease between 2019 and 2020 (7.8%). The territorial areas that need greater attention for the elimination of malaria are the North region, some foci in states in the Northeast and Midwest regions, in addition to micro foci in the Southeast and South regions.

Thus, actions and strategies must be thought out in a sectoral way, in view of the incidence of transmission risk. It is important to emphasize that information about malaria in Brazil may vary over time, in addition to underreporting on SINAN/DATASUS and Sivep-Malaria (not in the public domain) [51].

6. Conclusions

NTDs must be a permanent public agenda in all countries affected by them. Its control is essential to improve the health and well-being of the most vulnerable populations, reduce health inequalities, and achieve the global goals of sustainable development. It is a matter of social justice and a global responsibility, as well as ensuring access to adequate healthcare. The justifications for establishing a permanent agenda are:

1. Public health impact: NTDs primarily affect the most vulnerable populations in low-income countries, resulting in high rates of morbidity and mortality. Control of these diseases is essential to reduce human suffering and improve the quality of life of those affected.

2. Cycle of poverty and inequality: NTDs have a negative impact on the health of affected communities, leading to lost productivity, inability to work, and increased health care costs. This can lead to a decrease in family income, limiting access to education, food, and other basic resources.

3. Barriers to Accessing Health Care: NTDs affect populations that are in areas where health services are limited. Controlling these diseases requires strengthening health systems, improving access to diagnostic services and adequate treatment. This contributes to the reduction of inequities in access to health care.

4. Potential for control and elimination: adequate control of NTDs in the country can contribute to global elimination, bringing benefits to regional and global public health.

5. Impact on sustainable development goals: NTD control is included in the goals of the SDGs linked to health promotion, poverty reduction, gender equality, and sustainable development.

Global warming and the Brazilian economic growth model characterized by the disorderly expansion of urban centers are some of the conditions for the maintenance of NTDs. These conditions, together with the low coverage of water supply and sanitary sewage infrastructure, added to the favorable climatic characteristics, establish a scenario that prevents, in the short term, the proposition of actions aimed at reducing the transmissibility and elimination of the diseases.

Brazil has an extensive territory with climatic variations, where the specificities of each region must be considered when proposing programs and action plans for NTDs, in order to prevent, reduce, monitor, and map these diseases in the country. For there to be a stagnation of this public health problem in the national territory, it is essential to have political will, and investments in basic infrastructure to improve the living conditions of communities in areas still deprived of these services. These actions must

meet the demographic and cultural characteristics of the population and the peculiarities of each region.

The participative posture of the community, based on changing habits, practices, attitudes, and behaviors, together with the integration of government agencies, institutions and social organizations can promote strategies and actions for the prevention and adequate control of injuries, in each social context. It is worth emphasizing the government's responsibility to delve deeper into the social, political, and economic determinants linked to the occurrence of endemic diseases and intervene appropriately in the control.

Brazil, in order to succeed in the individual and collective right to health, mainly regarding the reduction and prevention of NTDs, it is necessary to establish legislation that addresses them in a united way and groups by type of transmission to gather efforts and avoid waste of public investment by sectoring the illnesses. It is necessary to include NTDs in the Previne Brasil Program, which is financially stimulated by the Federal Government through the actions of municipalities regarding their performance in the Primary Health Care indicators. Monitoring the indicators means improving the quality of the service offered to the population and, in this context, the NTDs should be included in the same Program. It is worth noting the importance of efforts by states and municipalities in meeting these demands, as well as raising awareness and community participation.

Raising public awareness and strengthening public policies are essential for controlling and eliminating NTDs in Brazil. It is critical to keep policies up to date and adapted to changes in your epidemiology and emerging challenges.

Author details

Nádia Teresinha Schröder[1], Eliane Fraga Da Silveira[1], Letícia Thomasi Janhke Botton[1] and Eduardo Périco[2*]

1 Lutheran University of Brazil (ULBRA), Canoas, Brazil

2 University of Vale do Taquari (UNIVATES), Lajeado, Brazil

*Address all correspondence to: perico@univates.br

IntechOpen

References

[1] Valverde R. Doenças Negligenciadas. 2023. Available from: https://agencia.fiocruz.br/doen%C3%A7as-negligenciadas

[2] Zicker F, Albuquerque PC, Fonseca e Fonseca BP. Doenças tropicais negligenciadas: Uma agenda inacabada. Rio de Janeiro: Fundação Oswaldo Cruz; 2019. p. 45. Available from: https://saudeamanha.fiocruz.br/wp-content/uploads/2019/10/PJSSaudeAmanha_Texto0035_V03. pdf

[3] World Health Organization. Neglected Tropical Diseases. 16 January 2023. 2023. Available from: https://www.who.int/news-room/questions-and-answers/item/neglected-tropical-diseases#:~:text=NTDs%20include%3A%20Buruli%2

[4] Brasil. Ministério da Ciência, Tecnologia e Inovação. Ministério da Ciência, Tecnologia e Inovação. In: Secretaria de Políticas e Programas de Pesquisa e Desenvolvimento. Coordenação-Geral de Mudanças Globais de Clima. Terceira Comunicação Nacional do Brasil à Convenção-Quadro das Nações Unidas sobre Mudança do Clima. Vol. I. Brasília; 2016. p. 135. Available from: https://repositorio.mcti.gov.br/bitstream/mctic/4312/2/2016_terceira_comunicacao_nacional_brasil_convencao_quadro_nacoes_unidas_sobre_mudanca_clima_v1.pdf

[5] Brasil. Constituição da República Federativa do Brasil. 1988. Available from: https://www.planalto.gov.br/ccivil_03/constituicao/constituicao.htm.

[6] Vecchi ID, Garcia ML, Sobrinho LLP. O Princípio da Dignidade Humana e suas Projeções no Âmbito Laboral: Possibilidades e limites. Sequência. 2020;**85**:249-286. DOI: 10.5007/2177-7055.2020v41n85p249

[7] Filó MCS, Garcia V. O oportunismo do discurso neoliberal na escolha das políticas públicas federais brasileiras durante a crise da Covid-19. Revista de Direito Público. 2021;**18**(98):543-569. DOI: 10.11117/rdp.v18i98.4718

[8] Meurer IR, Coimbra ES. Doenças tropicais negligenciadas e seu contexto no Brasil. HU Revista. 2022;**48**:1-2. DOI: 10.34019/1982-8047.2022.v48.37905

[9] Hability. ODS 11: Conheça os Objetivos da ONU Para as Cidades. 2023. Available from: https://habitability.com.br/ods-11-conheca-o-objetivo-da-onu-para-as-cidades/?utm_source=google_pago&utm_medium=&utm_content=&gclid=EAIaIQobChMI1MeTjoCCgAMV50p_AB1nOAswEAAYASAAEgIpQfD_BwE

[10] Organização Pan-Americana da Saúde. Iniciativa da OPAS de eliminação de doenças: política para um enfoque integrado e sustentável visando as doenças transmissíveis nas américas. 57º Conselho Diretor, 71ª Sessão do Comitê Regional da OMS para as Américas; de 30 de setembro a 4 de outubro de 2019. Washington, DC: OPAS; 2019. Available from: https://www.paho.org/sites/default/files/2020-01/2019-cde-dc57-elimin-init-framework-pt.pdf

[11] World Health Organization. Global Vector Control Response 2017-2030. Geneva: WHO; 2017. p. 64. Available from: https://www.who.int/publications/i/item/9789241512978

[12] Instituto Brasileiro de Geografia e Estatística. IBGE Cidades. 2022. Available from: https://cidades.ibge.gov.br/brasil/panorama

[13] Penso-Campos JM, Silveira EF, Caldas E, Sommer JAP, Périco E. Aspectos da paisagem e fatores socioeconômicos nos casos de dengue na cidade de Porto Alegre. RS. Revista Brasileira de Geografia Física. 2018;**11**(5):1846-1858. DOI: 10.26848/rbgf.v11.5.p1846-1858

[14] Veiga GS, Marquetti CP, Silveira EF, Sommer JAP. Hanseníase no Maranhão: distribuição espacial de 2013 a 2017. Revista de Iniciação Científica da Ulbra. 2021;**19**:1-6. DOI: 10.4322/ic.v1i19.7041

[15] Cafieiro TM, Sodré NS, Sommer JAP, Silveira EF, Schröder NT. Análise epidemiológica da Esquistossomose Mansônica nas regiões do Brasil. Research, Society and Development. 2022;**11**(2):e31011225579. DOI: 10.33448/rsd-v11i2.25579

[16] Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Vigilância em Saúde: Dengue, Esquistossomose, Hanseníase, Malária, Tracoma e Tuberculose. 2. ed. rev ed. Brasília: Ministério da Saúde; 2008. p. 197. (Série A. Normas e Manuais Técnicos) (Cadernos de Atenção Básica, n. 21). Available from: https://bvsms.saude.gov.br/bvs/publicacoes/cab_n21_vigilancia_saude_2ed_p1.pdf

[17] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Guia de vigilância epidemiológica. 7th ed. Brasília: Ministério da Saúde; 2009. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/guia_vigilancia_epidemiologica_7ed.pdf

[18] Organização Pan-Americana da Saúde. Indicadores De Saúde: Elementos Conceituais E Práticos (Capítulo 3). 2023. Available from: https://www3.paho.org/hq/index.php?option=com_content&view=article&id=14406:health-indicators-conceptual-and-operational-considerations-section-3&Itemid=0&showall=1&lang=pt#gsc.tab=0

[19] Brasil. Ministério da Saúde. Ministério da Educação. Guia de bolso do Programa Saúde na Escola: doenças negligenciadas. Brasília: Ministério da Saúde; 2022. p. 43. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/guia_saude_escola_doen%C3%A7as_negligenciadas.pdf

[20] Organização Pan-Americana da Saúde. Atenção primária à Saúde. 2023. Available from: https://www.paho.org/pt/topicos/atencao-primaria-saude

[21] Agência Nacional de Vigilância Sanitária (Anvisa). Manual para o Sistema Nacional de Hemovigilância no Brasil (Revisão do "Marco Conceitual e Operacional da Hemovigilância: Guia para a hemovigilância no Brasil"). Brasília: ANVISA; 2022. p. 147. Available from: https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2022/manual_de_hemovigilancia__dez22-07-12-2022.pdf/view

[22] Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Implantação das Redes de Atenção à Saúde e outras estratégias da SAS. Brasília: Ministério da Saúde; 2014. p. 160. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/implantacao_redes_atencao_saude_sas.pdf

[23] Brasil. Ministério da Saúde. Fundação Nacional da Saúde (Funasa). Programa de Controle da Dengue. Brasília, DF: Funasa; 2002. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/pncd_2002.pdf

[24] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância

Epidemiológica. In: Programa Nacional de Controle da Hanseníase. Relatório de Gestão. maio de 2007 a dezembro de 2008. Brasília, DF: Ministério da Saúde; 2009. p. 95. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/programa_nacional_controle_hanseniase_relatorio_gestao_maio_2007_dezembro_2008.pdf

[25] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Manual de vigilância e controle da leishmaniose. 1st ed. 5. reimpr. Brasília: Ministério da Saúde; 2014. p. 120. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/manual_vigilancia_controle_leishmaniose_visceral_1edicao.pdf

[26] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Programa Nacional de Prevenção e Controle da Malária PNCM. Brasília: Ministério da Saúde; 2003. p. 132. (Série C. Projetos, Programas e Relatórios). Available from: https://bvsms.saude.gov.br/bvs/publicacoes/programa_nac_prev_malaria.pdf

[27] Associação Nacional de Hospitais Privados. A luta contra as doenças tropicais negligenciadas continua. 2020. Available from: https://www.anahp.com.br/noticias/a-luta-contra-as-doencas-tropicais-negligenciadas-continua/

[28] Organização Pan-Americana da Saúde. Dengue. 2023. Available from: https://www.paho.org/pt/topicos/dengue#:~:text=O%20mosquito%20Aedes%20aegypti%20%C3%A9,pelo%20resto%20de%20sua%20vida

[29] Organização Pan-Americana da Saúde. Guia para vigilância, prevenção, controle e manejo clínico da doença de Chagas aguda transmitida por alimentos. Rio de Janeiro: PANAFTOSA-VP/OPAS/OMS; 2009. p. 92. (Serie de Manuais Técnicos, 12) https://bvsms.saude.gov.br/bvs/publicacoes/guia_vigilancia_prevencao_doenca_chagas.df

[30] Martins-Melo FR, Ramos AN, Alencar CH, Heukelbach J. Mortality from neglected tropical diseases in Brazil, 2000-2011. Bulletin of the World Health Organization. 2016;**94**(2):103-110. DOI: 10.2471/BLT.15.152363

[31] Brasil. Ministério da Saúde. Portaria Nº 264, de 17 de fevereiro de 2020. Brasília, DF: Ministério da Saúde; 2020. Available from: https://bvsms.saude.gov.br/bvs/saudelegis/gm/2020/prt0264_19_02_2020.html

[32] Mendes EV. O cuidado das condições crônicas na atenção primária à saúde: o imperativo da consolidação da estratégia da saúde da família. Organização Pan-americana da saúde: Brasília; 2012. p. 512. Available from: https://iris.paho.org/handle/10665.2/49107

[33] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde Boletim Epidemiológico – Territorialização e vulnerabilidade para doença de Chagas crônica. Número Especial. 2022. Available from: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/especiais/2022/boletim-especial-de-doenca-de-chagas-numero-especial-abril-de-2022

[34] Avaria A, Ventura-Garcia L, Sanmartino M, Van der Laat C. Population movements, borders, and chagas disease. Memórias do Instituto Oswaldo Cruz. 2022;**117**:e210151. DOI: 10.1590/0074-02760210151

[35] Dias JCP et al. Brazilian consensus on chagas disease. Epidemiologia e Serviços de Saúde. 2015, 2016;**25**:7-86. DOI: 10.5123/S1679-49742016000500002

[36] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Departamento de Vigilância das Doenças Transmissíveis. Vigilância da Esquistossomose Mansoni: diretrizes técnicas. 4th ed. Brasília: Ministério da Saúde; 2014. p. 144. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/vigilancia_esquistossome_mansoni_diretrizes_tecnicas.pdf

[37] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância das Doenças Transmissíveis. Educação em saúde para o controle da esquistossomose. Brasília: Ministério da Saúde; 2018. p. 40. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/educacao_saude_controle_esquistossomose.pdf

[38] Organização Pan-Americana da Saúde. Brasil Fortalece Capacidade de Diagnóstico da Hanseníase. 2022. Available from: https://www.paho.org/pt/noticias/25-1-2022-brasil-fortalece-capacidade-diagnostico-da-hanseniase

[39] Organização Mundial da Saúde. Diretrizes para o Diagnóstico, Tratamento e Prevenção da Hanseníase. Nova Deli: Organização Mundial da Saúde, Escritório Regional do Sudeste Asiático; 2019. Available from: https://www.paho.org/pt/documents/guidelines-diagnosis-treatment-and-prevention-leprosy

[40] Organização Mundial da Saúde. Estratégia Global de Hanseníase 2021-2030 "Rumo à zero hanseníase". Nova Delhi: Organização Mundial da Saúde, Escritório Regional para o Sudeste Asiático; 2021. Available from: https://www.who.int/pt/publications/i/item/9789290228509

[41] Brasil. Presidência da República. Casa Civil. Subchefia para Assuntos Jurídicos. Lei Nº 9.010 de 29 de março de 1995. Dispõe sobre a terminologia oficial relativa à hanseníase e dá outras providências. Brasília, DF: Presidência da República; 1995. Available from: https://www.planalto.gov.br/ccivil_03/leis/l9010.htm#:~:text=LEI%20N%C2%BA%209.010%2C%20DE%2029,Art

[42] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Estratégia Nacional para o Enfrentamento da Hanseníase 2019-2022. Brasília: Ministério da Saúde; 2021. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/estrategia_nacional_enfrentamento_hanseniase_2019.pdf

[43] Fundação Oswaldo Cruz. Políticas Públicas e Modelos de Atenção e Gestão à Saúde no PMA. Rio de Janeiro: Fiocruz; 2023. Available from: https://portal.fiocruz.br/politicas-publicas-e-modelos-de-atencao-saude-no-pma

[44] Organização Pan-Americana da Saúde. Leishmaniose. 2023. Available from: https://www.paho.org/pt/topicos/leishmaniose

[45] Silva DPC, Schröder NT, Silveira EF. Análise epidemiológica da Leishmaniose Visceral Humana no Brasil. In: Camargo LMA, Oliveira J, Meneguetti DUO, editors. Atualidades em medicina tropical na América do Sul: epidemiologia e educação em saúde. 1ª edição ed. Rio Branco: Stricto Sensu; 2021. pp. 9-24. DOI: 10.35170/ss.ed.9786586283563.01

[46] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Manual de vigilância e controle da leishmaniose visceral. Brasília: Editora do Ministério da Saúde; 2006. p. 120. (Série A. Normas e Manuais Técnicos). Available from: https://bvsms.

saude.gov.br/bvs/publicacoes/manual_vigilancia_controle_leishmaniose_visceral.pdf

[47] Portela G. Eutanásia em cães com leishmaniose é a melhor opção? Rio de Janeiro: Fiocruz; 2016. Available from: https://www.icict.fiocruz.br/content/eutan%C3%A1sia-em-c%C3%A3es-com-leishmaniose-%C3%A9-melhor-op%C3%A7%C3%A3o

[48] Ponte G. Saiba Como Prevenir as Leishmanioses. Rio de Janeiro: Fiocruz; 2022. Available from: https://portal.fiocruz.br/noticia/saiba-como-prevenir-leishmanioses

[49] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Imunização e Doenças Transmissíveis. Guia de tratamento da malária no Brasil. Brasília: Ministério da Saúde; 2020. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/guia_tratamento_malaria_brasil.pdf

[50] Organização Pan-Americana da Saúde. Malária. 2023. Available from: https://www.paho.org/pt/topicos/malaria

[51] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Imunização e Doenças Transmissíveis. Elimina Malária Brasil: Plano Nacional de Eliminação da Malária. Brasília: Ministério da Saúde; 2022. p. 60. Available from: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/svsa/malaria/politicas-de-saude/elimina-malaria-brasil-plano-nacional-de-eliminacao-da-malaria

[52] Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Ações de controle da malária: manual para profissionais de saúde na atenção básica. Brasília: Editora do Ministério da Saúde; 2006. p. 52. (Série A. Normas e Manuais Técnicos). Available from: https://bvsms.saude.gov.br/bvs/publicacoes/acoes_controle_malaria_manual.pdf

Chapter 5

Use of Spatial Epidemiology in Neglected Tropical Diseases Control, Elimination and Eradication

Kingford Chimfwembe, Christopher Simoonga, Hikabasa Halwindi and Rockiner Simoonga

Abstract

The burden of disease due to neglected tropical diseases in tropical and sub-tropical regions of the world still remains enormous. The diseases are prevalent in poor and marginalized communities where water and sanitation are a challenge and these communities are still grappling with other challenges like unemployment and other diseases. Africa shares the greatest burden of these diseases with women and children being the worst hit. In an effort to reduce the impact that these diseases have had on humans, global commitments and targets have been set to collectively deal with these diseases. Crucial to these global calls is epidemiological data showing exactly where these diseases occur so that the limited resources for control which is common in these poorer communities are targeted to areas where they will achieve maximum impact. Spatial epidemiology tools such as geographic information systems and remote sensing are therefore needed.

Keywords: neglected tropical diseases, control, spatial epidemiology, geographic information systems, remote sensing

1. Introduction

Neglected tropical diseases (NTDs) also known as diseases of poverty refer to a diverse group of diseases that cause serious morbidity and lead to mortality in the long term, especially in the poorest tropical and sub-tropical regions of the world [1]. These diseases are most prevalent in areas that are referred to as neglected because they do not receive much funding and attention compared to other diseases such as HIV, Malaria, Tuberculosis and now COVID-19 among others and the mechanisms under which they cause disease are not fully understood but are currently being studied just like most of the communicable diseases [1–3]. The epidemiology and transmission dynamic of these diseases are now being understood and this information is crucial for control, elimination and eradication [4]. NTDs include Buruli ulcer, Chagas diseases, Dengue and Chikungunya, Dracunculiasis (Guinea worm),

Echinococcosis, food-borne trematodes, Human African Trypanosomiasis (sleeping sickness), leishmaniasis, Leprosy (Hansen's disease), Lymphatic filariasis, Mycetoma, Onchocerciasis (river blindness), Rabies, Scabies, Schistosomiasis, Snakebite envenoming, Soil-transmitted helminthiases, Taeniasis/cysticercosis, Trachoma and Yaws (endemic treponematoses) diseases [2, 5].

NTDs affect approximately 1 billion of the total global population especially in low- and middle-income countries with Africa especially Sub-Saharan Africa accounting for approximately 40 to 51% of the total NTD burden [2, 6, 7]. They are not only responsible for health effects but also result in serious personal, social and economic impacts on populations [1] due to physical disabilities, disfigurement and blindness which lead to stigma, discrimination and loss of social status in adults and malnutrition, retarded growth and compromised cognitive development and school absenteeism in children [1, 7]. The mortality associated with NTDs is usually low compared to other infectious diseases and was estimated to be 242,000 in 2000 [8, 9].

2. Epidemiology of NTDs

The epidemiology of NTDs globally is determined by many factors, poverty and socioeconomic status being a major factor [10, 11] as it imparts on people's access to clean water and sanitation [12], quality education and its impact of behavioral factors key to NTD control [13] as well as general living conditions [14]. Other factors affecting the epidemiology and transmission dynamics of NTDs include war and conflicts [15] and weather and climate change which support the survival and distribution of the vectors for most of NTDs and restrict the distribution of most of the NTDs to the tropical and sub-tropical regions of the world [16]. Disturbance to the natural ecosystems due to rapid urbanization [10], globalization and international travel [17] and the mushrooming of cities with poor planning for sanitation [18] are other factors perpetuating the spread of NTDs.

The distribution of NTDs is prominent in the tropical and sub-tropical regions of Africa, Asia, Oceania, the Middle East and America [7, 19, 20]. In Africa, common NTDs include trachoma, ascariasis, hookworm, trichuriasis, lymphatic Filariasis, schistosomiasis including female genital schistosomiasis (FGS) [21], onchocerciasis, human African trypanosomiasis (HAT), loasis, leprosy and guinea worm [22–24]. They are predominantly found in West Africa; Nigeria, Chad, Niger, Mali and most of the Sahel region; Central Africa, Democratic Republic of Congo, Central African Republic, Sudan, Uganda and Angola and in Southern and Eastern African countries such as Zambia, Zimbabwe, Malawi, Mozambique and Tanzania [7, 20].

In Asia and Oceania, the NTDs are mostly found in India, Indonesia and China. This region has the highest burden of leprosy, lymphatic filariasis, soil-transmitted Helminthes, dengue and other arboviruses, yaws, scabies, trachoma, Japanese encephalitis and leishmaniasis [20, 25, 26] mostly in Indonesia and Papua New Guinea as well as India and South Asia. Although there is great success toward the elimination of schistosomiasis in China, which can also be true for soil-transmitted Helminthes since the treatment and control dynamics are the same, [27], China is known for food-borne trematodes such as clonorchiasis and paragonimiasis and other NTDs including trachoma and leprosy [26].

In the Middle East, the common NTDs are trachoma, leprosy, schistosomiasis, onchocerciasis, trichuriasis, rift valley fever, fascioliasis, soil-transmitted Helminthes and leishmaniasis [28]. These are found in parts of North Africa and

the Sahel region (Morocco, Algeria, Libya and Egypt), Yemen, Oman, Saudi Arabia, Jordan, Syria and Iraq [20, 29].

The distribution of NTDs in the Americas is centered in the regions of Brazil and the Amazon region, Gran Chaco area and the Mesoamerica and Texas regions [20]. In parts of Brazil and the Amazon region, common NTDs include Chagas' disease, leishmaniasis, schistosomiasis, dengue fever, leprosy, onchocerciasis and lymphatic filariasis [30]. Lymphatic filariasis, Schistosomiasis, Onchocerciasis, Trachoma and Soil-transmitted helminthiases are common NTDs in the Gran Chaco region of the Americas comprising of Bolivia, Paraguay, northern Argentina and parts of Brazil. The Mesoamerica and Texas regions of the America are common for intestinal helminth infections, cysticercosis, cutaneous leishmaniasis, dengue and Chagas disease [31].

3. Control, elimination and eradication of NTDs

The interventions toward NTDs are enshrined in the local, regional and global commitments using holistic strategies aimed at preventing and reducing transmission, reducing morbidity and mortality and ultimately eliminating and eradicating these diseases as public health problems [32]. The specific strategies employed can vary depending on the type and prevalence of NTDs in a particular region [33]. Tailored approaches are often necessary to address the unique challenges presented by each disease in a given geographic area [34]. The interventions toward of NTDs are now shifting from traditional approach, where it was only a responsibility of health departments in different countries, to a multi-sectoral approach. The current approach is anchored on collaboration involving governments, non-governmental organizations, pharmaceutical companies and international organizations which is critical for resource mobilization, technical expertise and coordination of efforts. Within counties, NTD interventions often require collaboration among health ministries, education, water and sanitation departments and other sectors. A multi-sectoral approach is essential to address the root causes of NTDs, such as poverty and inadequate access to clean water and sanitation [35].

Previously, the major strategies in the interventions toward NTDs were centered around preventive chemotherapy treatment (PCT) through mass drug administrations (MDA) as well as individual case finding and management, which is also known as innovative and intensified disease management (IDM) for NTDs [36]. There is now a paradigm shift because the proposed NTD interventions strategies now have vector control and social science approaches [7, 37, 38].

The NTDs intervention through PCT involves large-scale administration of drugs to the identified population at risk without any need for diagnosis to confirm infection status [39]. The drugs are administered to the populations at risk and regular interval for a specified period time. It is highly recommended that MDAs are conducted in an integrated manner to maximize on the cost of conducting the programs and also increase the impact of the drugs used and improve health outcomes since NTD epidemiology in most settings shows an overlap and because some drugs used in MDAs on a particular NTD may also be effective against other NTDs [40–42]. The NTDs targeted under this strategy include lymphatic filariasis, onchocerciasis, trachoma, schistosomiasis and soil-transmitted helminthiasis [36]. For trachoma treatment, two antibiotics, 1% tetracycline eye ointment and azithromycin are recommended. The SAFE strategy (Surgery, Antibiotics, Facial cleanliness and Environmental improvement) is also applied in trachoma management [43].

Strategy	Commitment(s)
The London Declaration on NTDs (2012).	• Stakeholders agree to control, eradicate or eliminate 10 NTDs by 2020.
The Regional Strategy on Neglected Tropical Diseases in the WHO African Region (document afr/rc63/10); AFR/RC63/R6, Sept. 2013.	• Country ownership and leadership of NTDs. • Broad-based national and international coordination and collaboration on NTDs. • Empowerment of people and communities in NTD control. • Evidence-based approach generated through scientific evidence mapping, monitoring, evaluation and research. • Strengthening health systems for NTDs. • Equity and gender-based interventions for NTDs [47].
The 66.12th World Health Assembly Resolution: WHA66., 2013.	• Prioritize prevention, control, elimination and eradication of NTDs in national health agendas. • Sustain the development and updating of evidence-based strategies for prevention, control and elimination of NTDs. • Collect additional information on the costing of interventions and of the socioeconomic impact NTDs. • Collaborate with partners in key areas to implement interventions to prevent and control NTDs. • Ensure predictable, long-term financing for sustained interventions against NTDs. • Build national capacity to implement preventive chemotherapy interventions. • Review programmatic progress in the preparation of strategic and operational plans for NTDs. • Intensify national control activities, harmonize strategies and control methods, for NTDs. • Improve coordination with related sectors on NTD.
The Addis Ababa NTD Commitment (2014)	• Work to increase domestic contribution to the implementation of NTD programs. • Promote a multi-sectoral approach in the implementation of NTD program goals. • Ensure the adoption of both long-range strategic and annual implementation plans for NTDs. • Report and use program data in a timely fashion. • Ensure that the implementation of NTD programs contributes to the strengthening the overall health system.
The 70th World Health Assembly (WHA) held in Geneva, Switzerland in May 2017.	Global Vector Control Response (2017–2030) adopted aimed at • Preventing, detecting, reporting and responding to outbreaks of vector-borne diseases; • Using an integrated approach when preventing, detecting, reporting and responding to outbreaks of vector-borne diseases.

Strategy	Commitment(s)
The 73rd World Health Assembly, WHA73; 13 November 2020.	• Member States to implement the new road map for neglected tropical diseases 2021–2030, "Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030". • Advocating for and providing technical assistance and guidance to Member States and partners in the implementation of the new road map for neglected tropical diseases 2021–2030 toward reaching Sustainable Development Goal target 3.3.
The 2021–2030 NTD Road Map (2020).	Facilitation of accelerated progress toward control, elimination, interruption of transmission, and eradication of NTDs through three strategic pillars of: • Accelerating programmatic action with a focus on impact rather than progress measures; • Intensifying cross-cutting approaches; • Changing operating models and culture to facilitate country ownership for NTD control.

Table 1.
Commitments toward NTDs prevention, control, elimination and eradication.

Single-dose albendazole (400 mg) or mebendazole (500 mg) are used during MDAs for the treatment of predominantly schoolgoing children against ascariasis and hookworms infections and in areas where trichuriasis may be present in addition to ascariasis and hookworm infections, ivermectin (IVM) is added to the combination of the drugs [44, 45]. IVM is also used in MDAs for onchocerciasis using a standard dose of 150–200 μg/kg, and in areas where onchocerciasis and LF are co-endemic, a combination of IVM and albendazole is used. For LF endemic areas, diethylcarbamazine (DEC) has been used in MDAs while for schistosomiasis, praziquantel (PZQ) is the drug of choice [44, 46].

The diseases considered under IDM control of NTDs include human African trypanosomiasis, leishmaniasis, Chagas diseases and Buruli ulcer [36]. Unlike PCT-based NTDs, where diagnosis is not a priority before treatment, IDM of NTDs is based on diagnosis and detection of disease to prompt treatment. These diseases demand a well-established health system with technical capacity at all levels to identify and diagnose these diseases [43].

Table 1 above shows some of the strategies for the control of NTDs with focus on the African region.

4. Use of spatial epidemiology in the control, elimination and eradication of NTDS

So far, interventions toward NTDs have, to a large extent, been centered on MDAs and IDM though other opportunities are emerging that can help regions affected by these diseases reach elimination and where possible eradication status [6, 7, 12, 20, 36, 39]. The success of these intervention programs depends on the availability of up-to-date and reliable information on the geographical distribution of the diseases. Recently, the development and application of tools such as geographic

information systems (GIS), remote sensing (RS) and spatial statistics have enhanced the understanding on the geographical distribution and mapping of NTDs [48–53]. The various ways through which GIS and RS technologies have been applied in NTDs interventions are discussed herein.

4.1 Disease distribution and hotspot identification

The distribution and hotspot identification of NTDs is essential in the determination of interventions and the maps that are developed using GIS and RS technologies depend on the nature of the NTD and the level of the intervention, whether it is control, elimination or eradication [54, 55]. Risk mapping is therefore a first stage in NTD interventions [56]. GIS and RS tools have been used in NTD control programs to map and show areas with the highest prevalence so that the resources for interventions which are usually scarce can be targeted at areas with the highest prevalence. Spatial statistics in a GIS system can also be used to estimate the numbers of the population at risk needing the intervention, information which is key to NTDs program managers [57, 58]. These strategies have been used for those NTDs that have been targeted for control using MDAs. NTDs that fall under IDM are targeted for elimination and therefore locations showing where actual transmission is taking place in GIS systems are required for application of the interventions and also for monitoring and evaluation purposes [55].

4.2 Mapping NTDs vector distribution

Vector-borne diseases account for a large proportion of all NTDs [37] and all vector-borne diseases combined account for about 17% of all communicable diseases. The distribution of vectors can be mapped using GIS so that areas that need control like the use of indoor residual spraying (IRS) and the distribution of mosquito nets can be prioritized in areas where there are more mosquitoes [59].

4.3 Predictive modeling of NTDs

Predictive modeling of NTDs using GIS and RS technologies has been used in cases where some data are available about the prevalence of the disease or vectors and such data are used to predict in other areas where the disease or vectors are likely to occur [51]. One approach is where RS data on environmental and climate factors affecting the distribution and survival of the vectors are used in a GIS system to generate hotspots for the distribution of NTDs [23, 24, 60]. In these studies, on NTDs, RS data such as temperature, precipitation, vegetation index alongside vector abundance and disease prevalence data have been used [61]. Using these approaches, spatial epidemiology can therefore be applied in developing early warning systems for NTD.

4.4 Climate change and disease modeling

There is evidence that climate change may affect the distribution of vector-borne diseases including NTDs [16, 62–65]. Remote sensing data can be used to study the effects of climate change on NTD transmission. Predictive models can help estimate future disease risks based on changing environmental conditions. GIS and RS technologies have been applied in predicting how climate change may impact on the geographical distribution of *Schistosoma japonicum, S. mansoni* and *S. haematobium* using

snail data. The developed model predicted that between 2021–2050 and 2071–2100, there could be an increase in the transmission of schistosomiasis [66] in some areas while other areas may also shrink in transmission.

4.5 Disease surveillance, monitoring and evaluation

As NTD interventions move into elimination and eradication stages, the use of spatial epidemiology will be a major advantage [6]. Through GIS, program managers can monitor whether the applied interventions over a specified period and depending on a particular NTD have been effective or not. This can be achieved by creating outputs in a GIS system showing changes in disease prevalence and transmission patterns over time. This will help evaluate whether the interventions have achieved the desired impact or not [67].

5. Conclusion

As control, elimination and eradication are prioritized in line with the WHO 2021–2030 roadmap for NTDs, risk maps before and after MDA and surveillance are needed. The use of GIS and RS technologies has potential to provide a clear understanding of the epidemiology and transmission dynamics of NTDs. This will lead to the production of maps highlighting the hotspots where interventions are needed. The potential use of GIS and RS in the modeling, mapping and control of NTDs in areas where these diseases are prevalent must therefore be emphasized. Critical to this is the building of capacity in spatial epidemiology especially in African settings where the capacities are still limited. There are still challenges with quality and up-to-date data on most NTDs in several settings and this may affect the quality of spatial outputs. With evidence that climate change may affect the distribution of NTDs transmitted by vectors, in situ studies on climate change are therefore proposed. More research is necessary to develop new tools, diagnostics and treatments for NTDs. The current spatial epidemiology tools must be evaluated and refined so that they can be applied in effective NTD control, elimination and eradication strategies. The possibility of using an integrated application of spatial epidemiology like in the case of malaria and lymphatic filariasis must be explored since the two diseases are transmitted by mosquito vectors. Comparative studies are also needed to compare the sensitivity and specificity of spatial epidemiology modelsdeveloped from using prevalence data against those developed using vector data only. Spatial models are also needed to show how the impact of using all the interventions for NTDs will perform in line with WHO 2021–2030 roadmap for NTDs.

Conflict of interest

The authors declare no conflict of interest.

Author details

Kingford Chimfwembe[1*], Christopher Simoonga[2], Hikabasa Halwindi[3] and Rockiner Simoonga[1]

1 Chreso University, Lusaka, Zambia

2 Ministry of Health, Lusaka, Zambia

3 University of Zambia, Lusaka, Zambia

*Address all correspondence to: kchimfwembe@yahoo.com

IntechOpen

References

[1] Ocholaid EA, Karanja DMS, Elliott SJ. The impact of neglected tropical diseases (Ntds) on health and wellbeing in sub-saharan Africa (ssa): A case study of Kenya. PLoS Neglected Tropical Diseases. 2021;**5**(2):1-19

[2] George NS, David SC, Nabiryo M, Sunday BA, Olanrewaju OF, Yangaza Y, et al. Addressing neglected tropical diseases in Africa: A health equity perspective. Global Healthcare Research Policy. 2023;**8**(1):30

[3] Hotez PJ, Molyneux DH, Fenwick A, Savioli L, Takeuchi T. A global fund to fight neglected tropical diseases: Is the G8 Hokkaido Toyako 2008 summit ready? PLoS Neglected Tropical Diseases. 2008;**2**(3):1-3

[4] World Health Organization. Accelerating Work to Overcome the Global Impact of Neglected Tropical Diseases: A Roadmap for Implementation. (No. WHO/HTM/NTD/2012.5). World Health Organization; 2012

[5] World Health Organization. Global Report on Neglected Tropical Diseases 2023. World Health Organization; 2023

[6] World Health Organisation. Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021-2030 [Internet]. 2020. Available from: http://apps.who.int/bookorders.

[7] Mitra A, Mawson A. Neglected tropical diseases: Epidemiology and global burden. Tropical Medical Infectious Diseases. 2017;**2**(3):36

[8] Horton R. GBD 2010: Understanding disease, injury, and risk. The Lancet. 2012;**380**(9859):2053-2054

[9] Hotez PJ, Alvarado M, Basáñez MG, Bolliger I, Bourne R, Boussinesq M, et al. The global burden of disease study 2010: Interpretation and implications for the neglected tropical diseases. PLoS Neglected Tropical Diseases. 2014;**8**(7):e2865

[10] Magalhães AR, Codeço CT, Svenning JC, Escobar LE, Van de Vuurst P, Gonçalves-Souza T. Neglected tropical diseases risk correlates with poverty and early ecosystem destruction. Infectious Diseases of Poverty. 2023;**12**(1):1-15

[11] Engels D, Zhou XN. Neglected tropical diseases: An effective global response to local poverty-related disease priorities. Infectious Diseases of Poverty. BioMed Central Ltd. 2020;**9**(10):1-9

[12] Boisson S, Engels D, Gordon BA, Medlicott KO, Neira MP, Montresor A, et al. Water, sanitation and hygiene for accelerating and sustaining progress on neglected tropical diseases: A new global strategy 2015-20. International Health. Oxford University Press. 2015;**8**:i19-i21

[13] Allotey P, Reidpath DD, Pokhrel S. Social sciences research in neglected tropical diseases 1: The ongoing neglect in the neglected tropical diseases. Health Research Policy and Systems. 2010;**8**(32):1-8

[14] Houweling TAJ, Karim-Kos HE, Kulik MC, Stolk WA, Haagsma JA, Lenk EJ, et al. Socioeconomic inequalities in neglected tropical diseases: A systematic review. PLoS Neglected Tropical Diseases. Public Library of Science. 2016;**10**:1-28

[15] Du RY, Stanaway JD, Hotez PJ. Could violent conflict derail the London

declaration on NTDs? PLoS Neglected Tropical Diseases. 2018;**12**(4):e0006136

[16] Githeko AK, Lindsay SW, Confalonieri UE, Patz JA. Climate change and vector-borne diseases: A regional analysis. Bulletin of the world health organization. 2000;**78**(9):1136-1147

[17] Norman FF, Pérez de Ayala A, Pérez-Molina JA, Monge-Maillo B, Zamarrón P, López-Vélez R. Neglected tropical diseases outside the tropics. PLoS Neglected Tropical Diseases. 2010;**4**(7):e762

[18] Hotez PJ. Global urbanization and the neglected tropical diseases. PLoS Neglected Tropical Diseases. Public Library of Science. 2017;**11**:1-5

[19] Casulli A. New global targets for ntds in the who roadmap 2021-2030. PLoS Neglected Tropical Diseases. 2021;**15**(5):1-10

[20] Hotez PJ. Ten global "hotspots" for the neglected tropical diseases. PLoS Neglected Tropical Diseases. 2014;**8**(5):1-3

[21] Kjetland EF, Leutscher PDC, Ndhlovu PD. A review of female genital schistosomiasis. Trends in Parasitology. 2012;**28**(2):58-65

[22] Schur N, Hürlimann E, Garba A, Traoré MS, Ndir O, Ratard RC, et al. Geostatistical model-based estimates of schistosomiasis prevalence among individuals aged ≤20 years in West Africa. PLoS Neglected Tropical Diseases. 2011;**5**(6):1-17

[23] Stensgaard AS, Utzinger J, Vounatsou P, Hürlimann E, Schur N, Saarnak CFL, et al. Large-scale determinants of intestinal schistosomiasis and intermediate host snail distribution across Africa: Does climate matter? Acta Tropica. 2013;**128**(2):378-390

[24] Schur N, Hürlimann E, Stensgaard AS, Chimfwembe K, Mushinge G, Simoonga C, et al. Spatially explicit Schistosoma infection risk in eastern Africa using Bayesian geostatistical modelling. Acta Tropica. 2013;**128**(2):365-377

[25] Lahariya C, Pradhan SK. Can Southeast Asia eradicate yaws by 2010? Some lessons from the yaws eradication programme of India. National Medical Journal of India. 2007;**20**(2):81-86

[26] Narain JP, Dash AP, Parnell B, Bhattacharya SK, Barua S, Bhatia R, et al. Elimination of neglected tropical diseases in the South-East Asia Region of the World Health Organization. Bulletin of the World Health Organization. 2010;**88**:206-210

[27] Wang W, Bergquist R, King CH, Yang K. Elimination of schistosomiasis in China: Current status and future prospects. PLoS Neglected Tropical Diseases. 2021;**15**(8):e0009578

[28] Hotez PJ, Savioli L, Fenwick A. Neglected tropical diseases of the middle East and North Africa: Review of their prevalence, distribution, and opportunities for control. PLoS Neglected Tropical Diseases. 2012;**6**(2):1-8

[29] Miller DA. Neglected tropical diseases—Middle East and North Africa. Clinical Infectious Diseases. 2015;**61**(5):857-857

[30] Lindoso JAL, Lindoso AABP. Neglected tropical diseases in Brazil. In: Revista do Instituto de Medicina Tropical de Sao Paulo. Vol. 51. Brazil: Instituto de Medicina Tropical de Sao Paulo; 2009. pp. 247-253

[31] Hotez PJ, Bottazzi ME, Dumonteil E, Valenzuela JG, Kamhawi S, Ortega J, et al. Texas and Mexico: Sharing a legacy of poverty and neglected tropical diseases. PLoS Neglected Tropical Diseases. 2012;**6**(3):1-6

[32] Bodimeade C, Marks AM, Mabey D. CME: TROPICAL MEDICINE neglected tropical diseases: Elimination and eradication. Clinical Medicine. 2019;**19**(2):157-160. Available from: www.who.int/neglected_diseases/mediacentre/

[33] Kelly-Hope LA, Sanders AM, Harding-Esch E, Willems J, Ahmed F, Vincer F, et al. Complex emergencies and the control and elimination of neglected tropical diseases in Africa: Developing a practical approach for implementing safe and effective mapping and intervention strategies. Conflict and Health. 2021;**15**(1):1-12

[34] Nina S, Joseph J, Amon. Addressing inequity: Neglected tropical diseases and human rights. Health and Human Rights Journal. 2018;**20**(1):11-25

[35] Ackley C, Elsheikh M, Zaman S. Scoping review of neglected tropical disease interventions and health promotion: A framework for successful NTD interventions as evidenced by the literature. PLoS Neglected Tropical Diseases. 2021;**15**(7):e0009278

[36] Rosenberg M, Utzinger J, Addiss DG. Preventive chemotherapy versus innovative and intensified disease management in neglected tropical diseases: A distinction whose shelf life has expired. PLoS Neglected Tropical Diseases. 2016;**10**(4):1-4

[37] World Health Organization. Multisectoral Approach to the Prevention and Control of Vector-Borne Diseases: A Conceptual Framework. 2020

[38] Reidpath DD, Allotey P, Pokhrel S. Social sciences research in neglected tropical diseases 2: A bibliographic analysis. Health Research Policy System. 2011;**9**(1):1-12

[39] World Health Organization. Preventive Chemotherapy in Human Helminthiasis. Coordinated Use of Anthelminthic Drugs in Control Interventions: A Manual for Health Professionals and Programme Managers. France: World Health Organization; 2006. 1-62 p

[40] Simpson H, Mengiste A, Mbonigaba JB, Kollie K, Nganda M, Dean L, et al. Research priorities to support the development of integrated national strategies to control skin-neglected tropical diseases. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2023;**117**(2):132-138

[41] Hotez PJ, Velasquez RM, Wolf JE. Neglected tropical skin diseases. JAMA Dermatology. 2014;**150**(5):481

[42] Mohammed KA, Deb RM, Stanton MC, Molyneux DH. Soil transmitted helminths and scabies in Zanzibar, Tanzania following mass drug administration for lymphatic filariasis – a rapid assessment methodology to assess impact. Parasites & Vectors. 2012;**5**(1):299

[43] Forbes K, Basáñez MG, Hollingsworth TD, Anderson RM. Introduction to the special issue: Challenges and opportunities in the fight against neglected tropical diseases: A decade from the London declaration on NTDs. Philosophical Transactions of the Royal Society B: Biological Sciences. 2023;**378**(1887):1-18

[44] Webster JP, Molyneux DH, Hotez PJ, Fenwick A. The contribution of mass drug administration to global

health: Past, present and future. Philosophical Transactions of the Royal Society B: Biological Sciences. 2014;**369**(1645):20130434

[45] Speich B, Ame SM, Ali SM, Alles R, Huwyler J, Hattendorf J, et al. Oxantel pamoate–albendazole for *Trichuris trichiura* infection. New England Journal of Medicine. 2014;**370**(7):610-620

[46] Taylor MJ, Hoerauf A, Bockarie M. Lymphatic filariasis and onchocerciasis. The Lancet. 2010;**376**(9747):1175-1185

[47] World Health Organization. Regional strategy on neglected tropical diseases in the WHO African region 2014-2020. 2013;**80**(932020):20. Available from: https://www.afro.who.int/sites/default/files/2017-06/regional-strategy-on-neglected-tropical-diseases-in-the-who-african-region-2014%E2%80%932020%20%281%29.pdf

[48] Sturrock HJW, Pullan RL, Kihara JH, Mwandawiro C, Brooker SJ. The use of bivariate spatial Modeling of questionnaire and parasitology data to predict the distribution of Schistosoma haematobium in coastal Kenya. PLoS Neglected Tropical Diseases. 2013;**7**(1):1-11

[49] Sturrock HJW, Gething PW, Ashton RA, Kolaczinski JH, Kabatereine NB, Brooker S. Planning schistosomiasis control: Investigation of alternative sampling strategies for Schistosoma mansoni to target mass drug administration of praziquantel in East Africa. International Health. 2011;**3**(3):165-175

[50] Turner HC, Truscott JE, Fleming FM, Hollingsworth TD, Brooker SJ, Anderson RM. Cost-effectiveness of scaling up mass drug administration for the control of soil-transmitted helminths: A comparison of cost function and constant costs analyses. The Lancet Infectious Diseases. 2016;**16**(7):838-846

[51] Simoonga C, Utzinger J, Brooker S, Vounatsou P, Appleton CC, Stensgaard AS, et al. Remote sensing, geographical information system and spatial analysis for schistosomiasis epidemiology and ecology in Africa. Parasitology. 2009;**136**:1683-1693

[52] Pullan RL, Bethony JM, Geiger SM, Cundill B, Correa-Oliveira R, Quinnell RJ, et al. Human helminth co-infection: Analysis of spatial patterns and risk factors in a Brazilian community. PLoS Neglected Tropical Diseases. 2008;**2**(12):1-9

[53] Magalhães RJS, Biritwum NK, Gyapong JO, Brooker S, Zhang Y, Blair L, et al. Mapping Helminth co-infection and co-intensity: Geostatistical prediction in Ghana. PLoS Neglected Tropical Diseases. 2011;**5**(6):1-13

[54] NTD Modelling Consortium, Achieving NTD Control, Elimination and Eradication Targets Post-2020 Modelling Perspectives and Priorities. Gates Open Research; 2019;**3**(1664):1664

[55] Brooker J, Jennifer S, Smith L. Mapping neglected tropical diseases: A global view. Community Eye Health. 2013;**26**(82):1

[56] Aula OP, McManus DP, Jones MK, Gordon CA. Schistosomiasis with a focus on Africa. Tropical Medicine and Infectious Disease. MDPI AG. 2021;**6**(109):1-40

[57] Queiroz JW, Dias GH, Nobre ML, De Sousa Dias MC, Araújo SF, Barbosa JD, et al. Geographic information systems and applied spatial statistics are efficient tools to study Hansen's disease (leprosy) and to determine areas of greater risk of disease. American Journal

of Tropical Medicine and Hygiene. 2010;**82**(2):306-314

[58] Simarro PP, Cecchi G, Franco JR, Paone M, Diarra A, Ruiz-Postigo JA, et al. Estimating and mapping the population at risk of sleeping sickness. PLoS Neglected Tropical Diseases. 2012;**6**(10):e1859

[59] Nihei N. Analysis of distribution of vector-borne diseases using geographic information systems. Nippon Eiseigaku Zasshi (Japanese Journal of Hygiene). 2017;**72**(2):123-127

[60] Stensgaard AS, Saarnak CFL, Utzinger J, Vounatsou P, Simoonga C, Mushinge G, et al. Virtual Globes and Geospatial Health: The Potential of New Tools in the Management and Control of Vector-Borne Diseases. 2009. c http://www.esri.com/software/arcgis/explorer/

[61] Costa J, Peterson AT. Ecological niche modeling as a tool for understanding distributions and interactions of vectors, hosts, and etiologic agents of Chagas disease. Recent advances on model hosts. 2011. pp. 59-70

[62] Booth M. Climate change and the neglected tropical diseases. In: Advances in Parasitology. United States: Academic Press; 2018. pp. 39-126

[63] Pandey BD, Costello A. The dengue epidemic and climate change in Nepal. The Lancet. Lancet Publishing Group. 2019;**394**:2150-2151

[64] Semenza JC, Suk JE. Vector-borne diseases and climate change: A European perspective. FEMS Microbiology Letters. 2018;**365**(2):1-9. Oxford University Press

[65] Tidman R, Abela-Ridder B, De Castañeda RR. The impact of climate change on neglected tropical diseases: A systematic review. Transactions of the Royal Society of Tropical Medicine and Hygiene. Oxford University Press. 2021;**115**:147-168

[66] Yang GJ, Bergquist R. Potential impact of climate change on schistosomiasis: A global assessment attempt. Tropical Medicine in Infectious Diseases. 2018;**3**(117):1-11

[67] Bergquist R, Yang GJ, Knopp S, Utzinger J, Tanner M. Surveillance and response: Tools and approaches for the elimination stage of neglected tropical diseases. Acta Tropica. 2015;**141**:229-234

Edited by Jorge Abelardo Falcón-Lezama and Roberto Tapia-Conyer

Despite enormous technical and scientific advances in medicine, neglected tropical diseases continue to be a major challenge in many regions of the world. As a result, the health systems of developing countries are overwhelmed by a double burden of disease, one represented by common health problems and another represented by these diseases. This situation generates wear and tear in all system components, making it ineffective, but also causes the gaps in health to become increasingly larger. This book provides general information on the problem of neglected tropical diseases. It is a current and updated reference to the problem in question that provides examples of the way in which health systems deal with neglected tropical diseases by seeking innovative solutions.

Published in London, UK

IntechOpen

ISBN 978-0-85466-069-8
9 780854 660698