# Neglected Tropical Diseases (NTD) in Worldwide and Its Significance in Health Care Services on Present Population

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Running Title: Neglected Tropical Diseases

Abstract: Neglected trophical diseases is one of the ignored diseases all over country leading to major area like Africa, Asia, America and India. Neglected tropical diseases (NTDs) are a diverse group of 20 conditions that are mainly prevalent in tropical areas, where they affect more than 1 billion people who live in impoverished communities. India has the world's largest absolute burden of at least 10 major NTDs, including hookworm, dengue, lymphatic filariasis, leprosy, visceral leishmaniasis or kala-azar and rabies. "NTDs continue to pose significant health burdens on some of the most disadvantaged communities in India. NTDs are found in several countries in Africa, Asia, and Latin America. NTDs are especially common in tropical areas where people do not have access to clean water or safe ways to dispose of human waste. The following six NTDs can be controlled or even eliminated through mass administration of safe and effective medicines or other, effective interventions: Dracunculiasis (Guinea Worm Disease), Lymphatic Filariasis, Onchocerciasis, Schistosomiasis, Soil-transmitted Helminths (STH) (i. e., Ascaris, Hookworm, and Whipworm), Trachoma etc. Controlling the vectors (e. g., mosquitoes, black flies) that transmit these diseases and improving basic water, sanitation, and hygiene are highly effective strategies against these NTDs.

Keywords: Trans abdominal pre peritoneal, TAPP, Fixation of Mesh, Complication

### 1. Introduction

Neglected tropical diseases (NTDs) caused by bacteria, viruses, worms, and other parasites afflict 1.4 billion of the world's poorest people, trapping them in a cycle of poor health, disability, and poverty. The World Health Organization (WHO) has targeted a group of these diseases for control, elimination, or eradication, and many institutions that support global health and international development, including PATH, have joined the effort. A pressing need for programs addressing NTDs is the availability of highquality, low-cost diagnostic tools deployable in low-resource settings. Tools that enable rapid and accurate detection of these diseases will become increasingly important for monitoring progress as levels of infection are reduced through disease-control efforts. Appropriate diagnostic tools also are needed to conduct surveillance for disease reemergence after presumed elimination.

Neglected tropical diseases (NTDs) are a diverse group of 20 conditions that are mainly prevalent in tropical areas, where they affect more than 1 billion people who live in impoverished communities. They are caused by a variety of pathogens including viruses, bacteria, parasites, fungi and

toxins. These diseases cause devastating health, social and economic consequences to more than one billion people.

The epidemiology of NTDs is complex and often related to environmental conditions. Many of them are vector-borne, have animal reservoirs and are associated with complex life cycles. All these factors make their public-health control challenging.

### 2. Definition

**Neglected tropical diseases (NTDs)** are a diverse group of tropical infections that are common in low-income populations in developing regions of Africa, Asia, and the Americas. They are caused by a variety of pathogens, such as viruses, bacteria, protozoa, and parasitic worms (helminths). These diseases are contrasted with the "big three" infectious diseases (HIV/AIDS, tuberculosis, and malaria), which generally receive greater treatment and research funding. In sub-Saharan Africa, the effect of neglected tropical diseases as a group is comparable to that of malaria and tuberculosis. NTD co-infection can also make HIV/AIDS and tuberculosis more deadly

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## **Neglected Tropical Diseases**



### List of NTD develop-S

There is some debate among the WHO, CDC, and infectious disease experts over which diseases are classified as neglected tropical diseases. Feasted, a researcher in neglected tropical diseases, notes 13 neglected tropical diseases:

- 1) Ascariasis,
- 2) Buruli Ulcer,
- 3) Chagas Disease,
- 4) Dracunculiasis,
- 5) Hookworm Infection,
- 6) Human African Trypanosomiasis,
- 7) Leishmaniasis,
- 8) Leprosy,
- 9) Lymphatic Filariasis,
- 10) Onchocerciasis,
- 11) Schistosomiasis,
- 12) Trachoma,
- 13) Trichuriasis.

Fenwick recognizes 12 "core" neglected tropical diseases: the same as above, excluding hookworm.

These diseases result from four different classes of causative pathogens:

- 1) Protozoa (for Chagas disease, human African trypanosomiasis, and leishmaniases);
- 2) Bacteria (for Buruli ulcer, leprosy, trachoma, and yaws),
- Helminths or metazoan worms (for cysticercosis/ taeniasis, dracunculiasis, echinococcosis, foodborne trematodiases, lymphatic filariasis, onchocerciasis, schistosomiasis, and soil-transmitted helminthiasis); and
- 4) Viruses (dengue and chikungunya, rabies)

### Area of NTD Develop-

- 1) NTDs flourish mainly in rural areas, in conflict zones and hard-to reach-regions.
- 2) They thrive in areas where access to clean water and sanitation is scarce worsened by climate change.
- 3) Furthermore, NTDs tend to affect regions without quality healthcare, leaving poor populations vulnerable

to these often debilitating diseases and newly emerging threats.

#### **Diagnostic Measure-**

- 1) NTDs are usually diagnosed during pregnancy, through laboratory or imaging tests.
- 2) Prenatal laboratory tests may include: "Triple screen" blood test: One part of the triple screen blood test looks for an elevated level of alpha-fetoprotein (AFP), which is associated with a higher risk of NTDs.
- 3) Owing to the advantages of PoC tests, they are highly preferred for diagnosing NTDs in resource-limited settings.

### **Preventive Measures-**

- 1) Neglected tropical diseases (NTDs) are largely preventable, even without vaccines.
- 2) Clean water, sanitary food handling, and good hygiene can prevent diseases such as guinea-worm disease, schistosomiasis, soil-transmitted helminthiasis, and trachoma
- 3) Educating the at-risk population is also an important aspect of NTD prevention.
- 4) By controlling environmental factors that invite NTDs, people can reduce their risk. For instance, eliminating areas of standing water, where mosquitoes like to breed, will reduce the risk of mosquito-borne diseases, or sleeping under a treated bed net will reduce the risk of diseases carried by flies that circulate at night.
- 5) Travelers to areas where insect-borne NTDs are widespread should take care to wear protective clothing, use bug repellant, and sleep under a treated bed net.
- 6) Vector-borne NTDs—those that are spread by worms, flies, mosquitoes, or other hosts—can be prevented through control of the vectors themselves.
- 7) This can include mass spraying of insecticides in areas where the vectors breed or gather, killing them before they become parasite carriers. Scientists are also exploring ways to genetically alter the vectors so that they cannot carry the parasite. The genetically altered vectors would then be released into the population to

## Volume 12 Issue 4, April 2023

## <u>www.ijsr.net</u>

breed and spread their genetic abnormalities to future generations.

### **Control Measure**

- 1) Regional success has been largely achieved through mass drug administration campaigns delivered in all endemic communities annually.
- 2) For diseases with proven elimination strategies and tools, a focused approach continues to accelerate their elimination.
- 3) For control and elimination of many other diseases, however, efforts are needed to gradually shift from reliance on preventive chemotherapy to a whole-ofsystem approach with multisectoral interventions and service delivery.
- 4) This includes enhancing the water supply and sanitation coverage, delivering veterinary public health and vector-control interventions, and increasing access to vaccines and antisera for all vulnerable and affected populations in the Region.

### Challenge

The most frequently mentioned barriers to WASH and NTD integration included:

- 1) Differing programmatic objectives in the two sectors, including different indicators and metrics
- 2) A disproportionate focus on mass drug administration
- 3) Differences in the scale of funding
- 4) Siloed funding
- 5) A lack of coordination and information sharing between the two sectors. Participants also conveyed that a more holistic approach was needed if future integration efforts are to be scaled-up.

## The most commonly mentioned requisite conditions included:

- 1) Education and advocacy
- 2) Development of joint indicators
- 3) Increased involvement at the ministerial level
- 4) Integrated strategy development
- 5) Creating task forces or committed partnerships
- 6) Improved donor support.

### What are NTDS and where can be found

According to the WHO criteria for classification, NTDs are diseases, disorders, or conditions that (1) disproportionately affect poor and marginalized populations, causing important morbidity and mortality, therefore justifying a global response; (2) mainly affect, but are not limited to, communities living in tropical and subtropical areas, especially those far from healthcare settings; (3) can be prevented and controlled by public health interventions; and (4) are relatively neglected by scientific research and public/private funding, compared to the magnitude of the health problem

Based on the above criteria, WHO currently focuses on a diverse group of 20 diseases and disease groups, mainly infectious, caused by (lyssa-and arbo -) virus, bacteria, fungi, parasites (protozoa and helminths), and toxins (snake bite envenoming, noncommunicable disease), all of global public health importance. This priority list does not account

for all the neglected clinical conditions causing health, social, and economic burdens worldwide. For instance, *PLOS Neglected Tropical Diseases* has significantly expanded this list to include additional diseases or conditions with chronic and/or debilitating characteristics comparable to the core NTDs group

### Alphabetical list of currently endorsed NTDS in the portfolio of WHO \* [Synonymous] (forms of the same disease or diseases caused by different etiologic agents)

- Buruli ulcer
- Chagas disease [American trypanosomiasis]
- Dengue and Chikungunya
- Dracunculiasis [Guinea-worm disease]
- Echinococcosis (alveolar, cystic, neotropical)
- Foodborne trematode infections (clonorchiasis, opisthorchiasis, fascioliasis, paragonimiasis)
- Human African trypanosomiasis, HAT [sleeping sickness] (gambiense and rhodesiense forms)
- Leishmaniasis (cutaneous, mucocutaneous, visceral)
- Leprosy [Hansen disease]
- Lymphatic filariasis [Elephantiasis]
- Mycetoma, chromoblastomycosis, and other deep mycoses
- Onchocerciasis [river blindness]
- Rabies
- Scabies and other ectoparasitoses
- Schistosomiasis [bilharzia] (intestinal and urogenital)
- Soil-transmitted helminthiases, STHs (ascariasis, ancylostomiasis, necatoriasis, trichuriasis, strongyloidiasis)
- Snake bite envenoming
- Taeniasis and cysticercosis
- Trachoma
- Yaws (Endemic treponematoses)

Irrespective of classifications, the vast majority of NTDs are prevalent in tropical and subtropical regions of Africa, America, Asia, and Oceania. However, some of them historically extend beyond these borders. For example, cystic echinococcosis, alveolar leishmaniasis, and echinococcosis are historically endemic in Europe. The observed recrudescence of NTDs' presence out of core endemic areas can be attributed to global societal and climatic changes. Events such as human migration, international travel, animal movements and trade, food trade, economic downturns, and climate changes may extend the areas of presence of pathogens causing NTDs, their mammalian hosts, the transmission season, and competence of vectors, spreading NTDs worldwide. This is the case of some poverty-related protozoan and helminthic NTDs in southern United States and vector-borne NTDs and schistosomiasis in southern Europe. In the case of other arboviral NTDs, such as dengue and chikungunya, an autochthonous transmission cycle has now been established in southern Europe

## Main challenges, successes, and failures during last two decades

1) An alternative, pragmatic approach is to list NTDs on the basis of progresses and failures towards goals set for their prevention, control, elimination, and eradication.

## Volume 12 Issue 4, April 2023 www.ijsr.net

- A major part of the success in reducing the health, 2) social, and economic burden of NTDs can be attributed the historical implementation of integrated to programmes of mass drug administration (MDA, also referred to as preventive chemotherapy) focusing on single use or combination of mainly 5 drugs (albendazole or mebendazole, ivermectin, praziquantel, and azithromycin) targeting major soil-transmitted helminthiases (STHs; ascariasis, trichuriasis, ancylostomiasis, necatoriasis), lymphatic filariasis, onchocerciasis, schistosomiasis, and trachoma.
- 3) More recently, it has been noted that MDA might have collateral benefits on other conditions such as strongyloidiasis, scabies, loiasis, mansonelliasis, food borne trematodiases, taeniasis, and yaws. Since 2011, over 20 billion doses of quality-assured medicines for MDA were donated by the pharmaceutical companies to endemic countries to support control and elimination of NTDs, and more than 1 billion people/year have been treated for at least one disease for 5 consecutive years (2015 to 2019). Only in 2019, 2.7 billion treatments by means of MDA were delivered for NTDs.
- 4) In this context, WHO estimated that 500 million fewer people were in need of interventions in 2019 compared to 2010, with 42 countries having eliminated at least one of the 20 prioritized NTDs. Thanks to scale-up of interventions and progress made during the last decades, there are now 5 NTDs whose eradication, elimination, or elimination as a public health problem is on the horizon: dracunculiasis, gambiense form of Human African Trypanosomiasis (HAT), lymphatic filariasis, trachoma, and yaws.
- 5) The main goal for the control of the 2 major forms of schistosomiasis (intestinal and urogenital) is to reach by means of praziquantel MDA, more than 75% treatment coverage of school-aged children, at-risk adults, and communities living in highly endemic areas. In 2019, 77.8 million people (64.9 million school-aged children and 12.9 million adults) were treated by MDA for schistosomiasis, corresponding to 34.6% of those in need.
- 6) Although human deaths associated to dog-mediated rabies (95% of all-deaths from rabies) are estimated at around 23, 500 to 59, 000 per year, mostly children younger than 15 years living in Asia and Africa, elimination was achieved in Canada, Western Europe (in 2019, only Poland and Romania were reporting cases in European Union), USA, Japan, and substantial decrease in Latin American countries.
- 7) The highly committed "Zero by 30" global strategic plan to eliminate dog-mediated rabies is now in place, with the aim of guiding effective use of vaccines, medicines, and technologies, and generating both evidence-based guidance and high-quality data for control. Since 2010, total number of new leprosy cases declined by 27% after most endemic countries reached its elimination (defined as a prevalence rate of <1 case on treatment /10, 000 population) as a public health.
- 8) Since 2012, the number of reported cases of visceral leishmaniasis has slightly decreased globally and fallen significantly in Bangladesh, India, and Nepal, where the disease is targeted for elimination as a public health problem. A better access to diagnosis and treatment,

coupled with aggressive vector control strategies and elimination initiative in Asia, has led to these results; nevertheless, human conflicts and increased competence of vectors due to global warming have seen the rise of leishmaniasis in many areas, particularly the Middle East and East Africa

- 9) Sensible but less effective gains were obtained for some other NTDs, globally or in some specific geographic areas such as Latin America or Asia-Pacific region. Although vector control efforts progress in the Southern Cone of South America, challenges remain in the global fight against Chagas disease, which still affects around 6 to 8 million people worldwide, the vast majority in Latin America but also expanding in southern USA and Europe, mainly as nonvectorial transmission. Only 2 medicines are currently available for the treatment of Chagas disease (benznidazole and nifurtimox), both of which present serious side effects; in addition, their efficacy has been proved only during the early acute phase of infection, while benefits in the chronic phase are questionable.
- 10) In fact, the BENEFIT randomized study demonstrated that benznidazole administered after the onset of chronic Chagas cardiomyopathy does not alter the progression of heart disease, neither decrease mortality rate. New drug association, drug repositioning, research of new drug, and therapeutic vaccine are under evaluation for Chagas disease.

#### Ambitious targets for the WHO Roadmap 2021–2030

Ninety percent reduction in the number of people in need of treatment against NTDs, 75% reduction in DALYs related to NTDs, 100 countries having eliminated at least 1 NTD and at least 2 NTDs eradicated in the world. These are the overarching impact-oriented global targets set by WHO in the road map for NTDs 2021–2030 to achieve the Sustainable Development Goals (SDGs). This new WHO roadmap was developed through an extensive global consultation with NTDs stakeholders that began in 2018 and culminated in the endorsement of the document by 194 Member States at the 73rd World Health Assembly in November 2020.

WHO roadmap 2021–2030 also describes the integrated approaches needed to achieve these targets through cross-cutting activities built on 3 pillars:

Another distinct feature is to drive greater ownership by national and local governments, including communities.

The overarching 2030 global targets are:

- 1) Reduce by 90% the number of people requiring treatment for NTDs
- 2) Reduce by 75% the disability-adjusted life years (DALYs) related to NTD
- 3) Eliminate at least one NTD from 100 countries
- 4) Eradicate two diseases (dracunculiasis and yaws) globally
  - Accelerate actions aiming at reducing incidence, prevalence, morbidity, disability, and death due to NTDs by means of scientific advances, filling gap knowledge in research, providing new interventions

## Volume 12 Issue 4, April 2023

and effective, standardized, and affordable diagnostics.

- Intensify cross-cutting approaches by the integrated delivery of interventions that are common to several NTDs, mainstreaming them within national health systems in the context of universal health coverage, and enhancing coordination among stakeholders and related programmes such as WASH or vector control. Examples of these targets include: 75% reduction of deaths due to vector-borne NTDs, 75% MDA-integrated treatment coverage index, 40 countries adopting skin NTDs strategies, and 100% access to basic water supply, sanitation, and hygiene.
- Change operating models and culture to facilitate countries to take ownership of their NTD programmes. Examples of these targets include: 90% of endemic countries, collecting and reporting data on NTDs disaggregated by gender.

In the new road map, each NTD is differently targeted for eradication (dracunculiasis and yaws), interruption of transmission (HAT-gambiense form, leprosy, onchocerciasis), elimination as a public health problem (Chagas disease, HAT-rhodesiense form, visceral leishmaniasis, lymphatic filariasis, rabies, schistosomiasis, STHs, trachoma), and control (Buruli ulcer, dengue and echinococcosis, chikungunya, foodborne trematode mycetoma. infections, cutaneous leishmaniasis. chromoblastomycosis and other deep mycoses, scabies and other ectoparasitoses, snake bite envenoming, taeniasis, and cysticercosis). Primary and secondary targets have been identified for each NTD

## The future of NTD pandemics and the long wave of COVID-19

MDA remains a fundamental pillar for the concomitant control and elimination of NTD Pandemics which should therefore have been managed as synergistic epidemics. Nevertheless, the dark side of these interventions relies on the potential onset of (particularly anthelmintic) drug resistance that in the future may jeopardize all these global efforts. How to limit the environmental contamination of these drugs to avoid the insurgence of resistance is a relevant question, which has been too little debated in the scientific community. To circumvent this problem, new formulations and combination of more effective, soluble, age grouptargeted drugs are in the pipeline

### List of some new formulations and treatments of already existing drugs that have been recently developed and/or implemented against NTDs

- Alternative regimen of ivermectin, diethylcarbamazine citrate, and albendazole to shorten the duration of required interventions targeting lymphatic filariasis MDA
- Fexinidazole for the oral treatment of HAT (first stage and nonsevere second stage of gambiense form)
- Paediatric formulation of mebendazole by chewable tablets for the treatment of STHs
- Paediatric formulation of praziquantel under development for the treatment of schistosomiasis
- New paediatric formulations of benznidazole and nifurtimox for Chagas disease

- Egaten (triclabendazole) for the treatment of human fascioliasis. Licensed by the US Food and Drug Administration (FDA)
- Antibiotic therapy (oral rifampicin plus clarithromycin extended release) to replace surgery for treatment of Buruli ulcer in some cases
- Azithromycin for treatment of yaws (instead of injectable benzylpenicillin in most circumstances)
- Clinical trials of fosravuconazole for the treatment of mycetoma
- Moxidectin approved by the FDA for the oral treatment of human onchocerciasis in patients aged 12 years and older
- Oxfendazole in Phase I (SAD and MAD) and Phase II (safety and efficacy) clinical studies for the human use against cysticercosis and trichuriasis
- Patent on new enantiopure and racemic anthelmintic formulations of soluble "salts of compounds having benzimidazolic structure" in preclinical studies

In parallel, global health efforts should focus on core preventive interventions such as new vaccines production aiming at the interruption of the transmission rather than curative interventions, and new diagnostic tools for early diagnosis and monitoring of drug resistance. Frontrunners vaccines for dengue, schistosomiasis, leishmaniasis, Chagas disease, and onchocerciasis are advancing in clinical trials, and some will be licensed soon. WHO has also established an NTD Diagnostic Technical and Advisory Group (DTAG) to provide advice on diagnostics for control programmes and develop target product profiles for priority diagnostics. All these to be integrated into future MDA campaigns.

Moreover, the ongoing coronavirus disease 2019 (COVID-19) pandemic in tropical and subtropical areas might jeopardize these developments on NTDs. The long wave of COVID-19 is having an impact not only in terms of coinfections between SARS-CoV-2 and all pathogens causing NTDs but also on delay or suspension of MDA and other community-based activities such as health facility services, control programmes, early diagnosis, drug supply, routine surveillance, and population-based surveys.

The main public health consequences of these disruptions due to COVID-19 might be identified as an increased mortality and morbidity associated to NTDs and delays in achieving the goals set for the 2021-2030 roadmap on NTDs. On top of all this, a challenging question was raised at the beginning of this pandemic, whether COVID-19 would be the next NTD. According to "People's Vaccine Alliance, " such question would be reasonable, since it has been estimated that 90% of people from low-income countries would not have access to vaccines against COVID-19 in 2021, while 14% of the world population represented by rich countries have already optioned 53% production of the more promising vaccines. To overcome this vaccine nationalism, the COVAX partnership co-led by the triumvirate Vaccine Alliance (Gavi), the Coalition for Epidemic Preparedness Innovations (CEPI), and WHO is aiming at unbalancing this prediction, providing equitable access to vaccines at 2 billion people for the end of 2021

## Volume 12 Issue 4, April 2023

<u>www.ijsr.net</u>

### The Global Report on NTD 2023:

The *Global report on neglected tropical diseases 2023* provides a consolidated, up-to-date assessment of progress towards control, elimination and eradication of 20 diseases and disease groups (NTDs) globally, regionally and nationally. Progress is reported in the context of global

commitments, strategies and targets, which were determined through an extensive consultation that culminated in the endorsement of the document Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030 by the Seventy-third World Health Assembly in November 2020.



The document reports on the first two years of implementation of the road map (2021 and 2022). The information presented is based primarily on epidemiological and programmatic data for interventions conducted in 2021 and gathered in 2022, but the report also describes a wide range of activities and accomplishments that were registered in both 2021 and 2022; comparisons are often made against 2020 and 2019 data, especially with regard to COVID-19 disruptions.

The report shows that while progress has been made during the two years since the launch of the road map (2021-2022), hindrances in achieving the targets for 2030 have arisen and work to overcome these obstacles continues. These endeavours have also revealed the scale of the task and risk still facing communities affected by NTDs. WHO is committed to reporting on progress towards the targets NTD programmes set in the road map. This first progress report on the road map 2021–2030 provides an important benchmark in our collective accountability towards meeting set goals.

## 3. Future Plans

- The second World Neglected Tropical Diseases (NTDs) Day was celebrated on 30 January 2021.
- To mark the occasion, the World Health Organization (WHO) launched its roadmap for NTDs for the period 2021 to 2030, which is aimed at increasing prevention and control of these too-long neglected diseases.
- Described here is a global overview on past achievements, current challenges, and future prospects for the WHO NTDs roadmap 2021–2030.

## Volume 12 Issue 4, April 2023 www.ijsr.net

## 4. Conclusion

The notion of equity and primary health care is woven into the fabric of the global NTD agenda. NTD programmes mostly serve marginalized communities and prioritize the needs of the most disadvantaged groups of people that must be explicitly considered. NTD programmes are closely aligned with SDG targets and contribute to several of them. NTD interventions are often at the frontline of public health and are considered important steps on the path towards achieving UHC by 2030.

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