

Looking to social sciences to improve the control of neglected tropical diseases

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ABSTRACT

Neglected tropical diseases (NTDs) are a group of 17 infectious diseases with a wide range of symptoms and findings, affecting more than one billion people worldwide, mostly the poor. Over the past few years, the World Health Organization (WHO) and partners have committed to strengthening the fight against the NTDs by setting specific goals for control, elimination and eradication of the respective diseases. Mass drug administration (MDA) is an important strategy in the fight against several of the NTDs; however, in order to meet the WHO targets by 2020, high and sustained treatment coverage will be essential. Social sciences, a previously neglected aspect of NTD control programmes, could help strengthen and further develop MDA and the promotion of healthy behaviour. Lessons learned from other disease control programmes, such as the recent Ebola epidemic, could lend inspiration to the further fight against NTDs. In this review, we found only a limited number of primarily observational studies of social scientific approaches to the control of NTDs. There is a need for creative, yet robust studies to address the challenges of quantitatively measuring the effect of social sciences in a meaningful way. Qualitative studies of other global health challenges indicate that social sciences do have an important role to play, and medical, public health and social scientists will need to find ways of working together in order to successfully combat NTDs.

INTRODUCTION

The term ‘neglected tropical diseases’ (NTDs) includes a group of 17 infectious diseases caused by protozoa (American trypanosomiasis (Chagas disease), human African trypanosomiasis, leishmaniasis), helminths (cysticercosis/taeniasis, dracunculiasis, echinococcosis, foodborne trematodiasis, lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis), bacteria (Buruli ulcer, leprosy, trachoma, yaws) and viruses (dengue, rabies) [1]. Their disease presentation includes a wide range of symptoms and findings, and may affect multiple organ systems (Table 1).

NTDs affect more than one billion people worldwide and are responsible for a substantial global burden of disease, causing more than 26 million Disability-Adjusted Life Years (DALYs) annually [2, 3]. The impact of NTDs on individuals, families and communities in developing countries cause not only a huge burden of disease, but also impacts the quality of life and productivity. The diseases affect populations with low political visibility and voice, whose influence on decision and policy-making is minimal. The disfigurement and disability caused by NTDs particularly affects girls and women [4], contributing to gender-based inequality.

Disease	Main causative agents	Organs affected	Prevalence	1,000 DALYs (2010)*	Ref
American trypanosomiasis	<i>Trypanosoma cruzi</i>	Intracellular, systemic	7 million	546 (271–1,054)	[1, 3, 5]
Human African trypanosomiasis	<i>Trypanosoma brucei</i>	Blood, lymphatics, cerebrospinal fluid	6,314	560 (76–1,766)	[1, 3, 6]
Leishmaniasis	More than 20 species of <i>Leishmania</i>	CL: skin VL: systemic	1.3 million	3,317 (2,180–4,890)	[1, 3, 6]
Cysticercosis/ Taeniasis	<i>Taenia solium</i>	Muscle, skin, CNS, eyes	No data	503 (379–663)	[1, 3]
Dracunculiasis	<i>Dracunculus medinensis</i>	Large intestines, especially caecum	126	No data found	[6, 7]
Echinococcosis	<i>Echinococcus granulosus</i> <i>Echinococcus multilocularis</i>	Liver, lungs, CNS, bones, kidneys, spleen, muscles, retro-ocular space	30/100 000 person-years in endemic areas	144 (69–286)	[1, 3]
Foodborne trematodiasis	<i>Clonorchis sinensis</i> , <i>Opisthorchis felinus</i> , <i>Opisthorchis viverrini</i> , <i>Fasciola hepatica</i> <i>Echinostoma spp</i> <i>Fasciolopsis buski</i> <i>Paragonimus spp</i>	Liver, lungs, intestines	56 million	665 (479–859)	[1, 3, 8]
Lymphatic filariasis	<i>Wuchereria bancrofti</i> <i>Brugia malayi</i> <i>Brugia timori</i>	Lymphatics	120 million	2,775 (1,807–4,000)	[1, 3, 6]
Onchocerciasis	<i>Onchocerca volvulus</i>	Subcutaneous tissues	37 million	494 (360–656)	[1, 3, 6]
Schistosomiasis	<i>Schistosoma mansoni</i> <i>S. haematobium</i> <i>S. japonicum</i>	Urogenital tract, intestines, ectopic	249 million	3,309 (1,705–6,260)	[1, 3, 6]
Soil-transmitted helminthiasis	<i>Ascaris lumbricoides</i> <i>Trichuris trichiura</i> <i>Necator americanus</i> <i>Ancylostoma duodenale</i>	Lungs, intestines	1.7 billion	5,190 (2,980–8,810)	[1, 2, 9]
Buruli ulcer	<i>Mycobacterium ulcerans</i>	Skin	5,000	No data found	[1, 6]
Leprosy	<i>Mycobacterium leprae</i>	Skin and nerves	215,656	6 (3–11)	[1, 3, 6]
Trachoma	<i>Chlamydia trachomatis</i>	Conjunctiva	21 million	334 (243–438)	[1, 3, 6]
Yaws	<i>T. pallidum pertenue</i>	Skin	Approx. 60,000	No data found	[1, 10]
Dengue	<i>Aedes aegypti</i> <i>Ae. albopictus</i>	Systemic	390 million	825 (344–1,412)	[1, 3, 11]
Rabies	Rabies virus	CNS	Not known	1,462 (852–2,659)	[1, 3]

Table 1: Symptoms and findings of 17 neglected tropical diseases.

*In parentheses the 95% confidence interval, CL = cutaneous leishmaniasis, VL: visceral leishmaniasis, CNS = central nervous system

Despite the substantial disease burden, NTDs receive relatively limited attention from the international community, and thereby inadequate funding for research, including studies of diagnostic tools and novel treatment methods, compared to other comparable diseases such as human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), malaria and tuberculosis [12]. Still, the treatment of most NTDs is safe and relatively simple to administer, and treatment of multiple co-infections may be integrated [13]. Since 2007, the World Health Organization (WHO) has committed to strengthen the fight against NTDs, and a number of stakeholders worldwide have joined the partnership.

In 2012, a coalition of endemic country governments, pharmaceutical companies, and non-governmental organisations (NGOs) came together to commit to the fight against NTDs, in what has been named the London declaration on NTDs [14]. A WHO and partners roadmap was developed for targeted control and elimination of NTDs [15]. Here, we review the present global health strategies to fight these diseases, and the status of control and elimination targets set by WHO. We thereafter explore and discuss some of the gaps that need to be filled in order to achieve the goals set for 2020, in particular alternative approaches that include the integration of social sciences in the combat of NTDs.

PROGRESS OF CONTROL AND ELIMINATION

Ten NTDs are targeted for control, elimination or eradication by WHO and partners, and below we review them in order of burden of global DALYs [2].

Soil-transmitted helminthiases (STHs) are caused by a group of helminths including *Necator americanus* and *Ancylostoma duodenale* (hookworms), *Ascaris lumbricoides* (roundworm) and *Trichuris trichiura* (whipworm). STHs commonly lead to undernutrition and anaemia, stunted growth and may prevent cognitive development, although this can be difficult to detect for all STHs collectively at the community level [16]. The STHs are targeted for global control¹ by 2020 [1]. Up to 2 billion people are at risk of STHs worldwide, and 876 million of them are children [9]. Mass drug administration (MDA) of pre-school and school-age children with albendazole or mebendazole is currently the key strategy to fight these infections; however, studies indicate that also adults should be treated in order to adequately control these diseases [17]. The treatment coverage target for 2020 is at least 75% of pre-school and school-age children in endemic countries; however, in 2013, only about 50 and 40 % of at-risk preschool-age and school-age children, respectively, were treated worldwide [18]. Currently, only 27% of countries have reached these targets, and, alongside MDA, interventions to improve access to safe drinking water and improved sanitation, as well as health education for improved hygiene in at-risk populations, will be needed [19].

Visceral leishmaniasis is a disease transmitted through bites of infected sand-flies. The parasite, *Leishmania*, attacks the immune system, bone marrow and internal organs, such as the liver and spleen, and, if left untreated, is usually fatal within few years [20]. WHO has set

¹ Control is defined by WHO as: "The reduction of disease incidence, prevalence, intensity, morbidity, or mortality, or a combination of these, as a result of deliberate efforts. (...) Continued intervention measures may be required to maintain this reduction."

the target to eliminate² visceral leishmaniasis as a public health problem by 2020, and to significantly reduce associated morbidity and mortality in other endemic regions [1].

Approximately 300,000 new cases are detected annually, and Bangladesh, Brazil, Ethiopia, India, Nepal, South Sudan and Sudan account for 90% of those. Up to 50,000 deaths occur every year due to infection, and strategies to achieve elimination include early diagnosis and treatment with a single intravenous dose of liposomal amphotericin B, a drug which is thought to disrupt the parasitic membrane through drug-binding to parasite [21]. Other efforts include transmission interruption through the use of insecticides and community education to change risk behaviour [22]. From 2012 to 2013, the number of reported cases in the three highest-burden countries, Bangladesh, India, and Nepal, was reduced by 37%, 33% and 50%, respectively [1].

Schistosomiasis is caused by mainly three species of the parasitic worm *Schistosoma*, of which *S. haematobium* and *S. mansoni* are the two predominant species [23]. People are infected through contact with infested fresh water, contaminated with larvae from the intermediate snail hosts, and symptoms include abdominal pain, diarrhoea, bloody stools, haematuria, and genital symptoms such as haematospermia, cervicitis and sterility. The disease may lead to liver and kidney damage, and in long-standing cases, gastroesophageal varices or urinary bladder cancer [24]. Schistosomiasis is targeted for global control by 2020, and WHO urges endemic countries to treat at least 75% of all school-age children and at-risk adults in need of treatment through preventive chemotherapy with praziquantel [1]. However, in 2012, only 14% of the people in need of treatment received praziquantel worldwide [1], although unprecedented donations by pharmaceutical companies have provided enough

² Elimination is defined by WHO as: "The reduction to zero of the incidence (...) in a defined geographical area (...); continued actions to prevent re-establishment of transmission may be required."

praziquantel to treat all school-age children in need of treatment worldwide. Drug availability alone is therefore not enough to ensure that WHO coverage targets are reached [25].

Lymphatic filariasis (LF) is caused by mosquito-transmitted helminths that invade and damage the lymphatic system, causing disfiguring thickening of the skin and swelling (lymphedema) of the lower extremities (elephantiasis), scrotum (hydrocele) and female breasts [26]. The disease is targeted for global elimination by 2020 [1]. In 2013, at least 40 million people had clinical manifestations, whereas 1.4 billion people worldwide required preventive chemotherapy for LF. MDA is the core strategy to eliminate the disease, and a combination of albendazole and diethylcarbamazine (DEC) or ivermectin is used to break the transmission cycle through annual MDA [27]. Following five years of MDA, surveillance systems are put in place to verify the absence of disease transmission [1]. In 2013, over 400 million people worldwide were treated for LF [13]; however, in all African countries combined, the coverage was only 32% [28].

Human African trypanosomiasis is transmitted by infected Tsetse flies, and is mostly found in sub-Saharan Africa. Two types of protozoa cause chronic disease (*Trypanosoma brucei gambiense*, accounts for 98% of cases) and acute disease (*T. brucei rhodesiense*), respectively. Acute symptoms include fever and joint pain, and the parasite may invade the central nervous system, causing behavioural changes, confusion, sensory and sleep disturbances, giving the disease its more common name “sleeping sickness” [29]. The disease is targeted for global elimination by 2020 [1], and the number of infected individuals has gradually declined, with only 3,796 reported new cases in 2014, down 40% from 2013 [30]. Through the development and implementation of rapid diagnostic tests and more effective and simpler drugs, the target is fewer than 2,000 cases in 2020 [31].

American trypanosomiasis, or Chagas disease, is mostly found in rural Latin America. The disease is caused by the protozoa *T. cruzi*, and is transmitted through food, blood transfusions, and organ donations, and peripartum. The infection may lead to complications such as cardiomyopathy, megacolon and mega-oesophagus [32]. Chagas disease is targeted for global control by 2020 [1]. Around 6 million people are thought to be infected, and public health control strategies include organ and blood donation screening through the use of rapid diagnostic tests, and early anti-parasitic treatment of infected individuals [22]. In addition to these screening measures, elimination of disease-carrying insects in areas surrounding homes in Latin America are targeted for elimination by 2020 [33].

Onchocerciasis, also known as river blindness, is caused by the parasitic worm *Onchocerca volvulus* transmitted by blackflies. The flies breed in fast-flowing rivers, and in humans inflammation caused by the death of the parasite larvae leads to damage of the skin and eyes (cornea), resulting in severe skin itching and potentially blindness [34]. Onchocerciasis is targeted for elimination by 2015 in Latin America and Yemen, and by 2020 in selected countries in Africa [15, 16]. It is the world's second leading infectious cause of blindness, after trachoma, and an estimated 37 million people in sub-Saharan Africa are infected, representing 99% of the global burden of this disease [1]. MDA of ivermectin is used to interrupt transmission, and, since 1995, individuals in affected communities in Africa have been trained to distribute ivermectin to fellow community members through so-called community-directed treatment supplied through the African Programme for Onchocerciasis Control (APOC). In 2013, more than 100 million people were treated for onchocerciasis, and 12 African countries are expected to achieve elimination by 2020 [1]. In 2015, APOC

formally came to an end, and the challenge remains to sustain the high treatment coverage, such as through integration with other NTD control and elimination programmes [28].

Trachoma is caused by infection with the bacteria *Chlamydia trachomatis*, and is the most common cause of preventable blindness worldwide. The disease is targeted for global elimination by 2020 [1]. The so-called SAFE strategy has been put in place to ensure adequate measures of prevention and treatment are provided to at-risk populations: Surgery of trachomatous trichiasis³, Antibiotics (oral azithromycin) to treat on-going bacterial infections, Facial cleanliness to reduce transmission of disease, and Environmental improvements, such as access to safe water and sanitation facilities [35]. In 2015, more than 21 million people are estimated to have active trachoma and more than 230 million are at risk of infection [1]. In 2014, the WHO Alliance for the global elimination of trachoma by 2020 concluded that increased efforts are needed to ensure the F and E aspects of the SAFE strategy [36, 37].

Leprosy is caused by the bacteria *Mycobacterium leprae*, and is mainly spread through the air in droplets from infected individuals. The incubation period can be long, and the disease typically evolves in two stages; loss of sensation and muscle weakness, and thereafter permanent loss of vision and shortening of digits. The disease is targeted for global elimination by 2020 [1]. In 2013, more than 215,000 new leprosy cases were detected worldwide, and more than half of the cases are found in India alone. WHO focuses on early detection and antibiotic combination therapy in endemic countries, and the number of reported cases is declining steadily [1]. However, stigma caused by the disease may severely affect mental health, and can represent a major obstacle to early detection and treatment [38].

³ Corneal damage due to scraping by the lashes of inverted eyelids.

Guinea worm disease, or dracunculiasis, is caused by *Dracunculus medinensis*, also known as Guinea worm. Humans get infected through unclean drinking water containing water fleas infected with guinea worm larvae. The female larvae can grow to meter-long worms, emerging from the skin through painful blisters about a year after infection [39]. The disease is the only NTD targeted for eradication⁴ by 2020. There is no effective medicine or vaccine for the disease, and access to improved drinking water and promotion of healthy behaviour change are essential public health interventions. In the 1980s, Guinea worm disease was endemic in 20 countries with over 3 million cases every year, while in 2013, only 148 cases were found in five countries (Sudan, South Sudan, Chad, Ethiopia and Mali) [40]. During the first five months of 2015, only five cases were reported [41].

⁴ Eradication is defined by WHO as: "The permanent reduction to zero of the worldwide incidence of infection (...), with no risk of reintroduction."

STRENGTHENING CONTROL AND MOVING TOWARDS ELIMINATION

Current reports indicate a large variation in treatment coverage across the various NTDs targeted through MDA; schistosomiasis having the poorest global coverage with only 14% of those in need receiving treatment [1]. Onchocerciasis control programmes, on the other hand, have been successful in demonstrating the value of sustained, high treatment coverage in disease control, and potentially elimination [28]. In certain previously high-endemic areas, loss of eyesight has been completely eliminated as a cause of debilitating dysfunction [1].

Among the suggested success factors of sustained and high treatment coverage of onchocerciasis control programmes, the so-called community-directed treatment has been brought forward, and especially its local ownership, drug distribution on the premises of local communities, and limited or no financial incentives [42]. Although the successes of onchocerciasis control seem obvious best practices also for other NTD control programmes, the systematic use of lessons learned and scientific knowledge generation still lags behind as the control of NTDs needs to readjust if it is to achieve the 2020 WHO targets [43].

Health education for behaviour change

Appropriate health education is crucial for the success of most public health interventions, and has been shown to be essential also in global health programmes, although there is little evidence of the optimal format or frequency of such education [44]. A cluster-randomized trial in Uganda of behavioural change communication (BCC) for the use of insecticide-treated bed nets for malaria prevention found that additional health education beyond the standard programmatic BCC was not cost-effective [44]. Other studies suggest that the effect of the health intervention may increase with intensified health education, although cost-effectiveness analyses of these results are not clear [38, 45-48]. Few studies, and to our knowledge, only

one randomised controlled trial (RCT), have evaluated the effect and best practices for behaviour change in NTD control programmes. One RCT did not find any significant difference in health behaviour between groups participating and not in a short-term health education programme on schistosomiasis [49].

Ensuring treatment compliance

Treatment coverage surveys suggest that one of the main factors of successful MDA programmes is to appropriately address potential misconceptions of treatment, as well as the acceptance of often ill-tasting drugs with unwanted, mostly mild side effects [50-53]. Some have found that local communities may for example perceive western medicine as “witchcraft”, designed to make its members impotent or infertile [54]. Moreover, fear of side effects may prevent appropriate dosage, which in turn may lead to unwanted drug resistance [55, 56]. Also, when the drugs do not produce the same side effects as during initial treatment rounds, due to reduced parasite-associated symptoms, some may be led to believe the drugs are no longer efficient. No controlled, quantitative trials have been conducted to inform NTD control programmes of the most cost-efficient ways to ensure adherence to treatment.

Addressing the socio-political context

Some studies highlight the potential challenges of the wording of diseases and treatment in various languages, whereas others suggest that the gender of the drug distributors may affect treatment coverage results of MDA programmes [55]. Furthermore, NTD control programmes are required to take into account the socio-political context, not only in terms of safety and programme feasibility, but equally important, in terms of the local communities’ trust towards drug distributors and programme evaluators [57].

In line with the success of onchocerciasis control programmes, studies indicate that the involvement of local stakeholders and community leaders is essential to ensure community buy-in and treatment coverage [58, 59]. One review found that educating traditional healers could improve the capacities of the local community and their support of health programmes [60, 61].

DISCUSSION

The community-directed treatment of onchocerciasis (APOC) stands as an example of how the understanding of local social and cultural aspects may strengthen the control of infectious diseases. While the quantitative evidence of the effect of strategies such as health education to improve healthy behaviour and treatment adherence is scarce, qualitative data indicate that these efforts are worthwhile. Addressing the socio-political context in communities affected by NTDs is essential to the development of successful and efficient treatment programmes.

In order to ensure sustainable and cost-efficient treatment programmes, the control of NTDs needs to integrate social sciences' knowledge base of how social, cultural and physical environments may affect health behaviour [62, 63]. Despite successes such as APOC, social sciences, including medical anthropology, have not been widely integrated into the development of policies and decision-making of NTD control programmes. This might in part be due to the current drive for quantitative evidence of health effects of a given implementation or strategy, typical for evidence-based medical sciences [62].

Understanding the implications of social and cultural behaviour was essential to combat the recent Ebola epidemic in West Africa. A large number of individuals were infected through traditional burial rituals, which commonly involved physical contact with the deceased, and thereby contact with highly infectious material. Indeed, a study in Guinea showed that 85 confirmed Ebola cases could be linked to one single funeral ceremony in December 2014 [64]. As a consequence, mourning relatives were encouraged to abstain from traditional burial rituals, and in Sierra Leone, a campaign called "Safe Burials Save Lives" allowed professional burial teams to take care of the burial routines in a safe manner, while incorporating some ceremonial traditions where possible [65, 66]. However, the global health

community has been criticised for not addressing the essential social scientific aspects soon enough in the outbreak response, and that the development of appropriate health messages for the affected communities could have been more effective, and more lives saved, if medical anthropology had been integrated at an earlier point in time [67].

In the treatment of tuberculosis, one study investigated the effect of monthly vouchers of approximately \$15 which could be used in local shops for food. For those who received the voucher at least once, treatment success rates were significantly improved [68]. Other results suggest that food vouchers do not have an effect on improved outcomes [69]. The evidence is still limited, and challenges still remain with regard to scaling such interventions.

Several global health programmes have recently taken advantage of the rapid development of and access to technology, including the use of mobile phones and text message reminders to increase treatment adherence among targeted individuals [70, 71]. Even health workers' performance may be improved through text messages [72]. Recently, a study in Burkina Faso has been put in place to evaluate the effect of mass media interventions on health benefits through an RCT design [73]. The intervention population in this study is exposed to radio spots for 30 months, at least 10 times a day (so-called saturation approach), designed to stimulate various healthy behaviour changes, such as seeking treatment at clinics for fever and diarrhoea or saving money for an emergency during pregnancy. This intervention is being compared to control populations without exposure to the same radio spots. The midterm results, although not yet published in peer-reviewed literature, have so far shown significant improvements, especially in behaviours like seeking treatment for diarrhoea and taking oral rehydration therapy [38]. The long-term effects of various mass media interventions and their cost-effectiveness; however, have yet to be determined [45].

There still remains an untapped potential to leverage social sciences for BCC, health messaging and education campaigns in order to improving the effects of MDA programmes [74]. Studies suggest that even though MDA coverage may initially be high, this may not consistently lead to long-term treatment adherence [53, 56]. This could be due to fear of side effects, distrust of modern medicine, lack of perceived need for treatment, or simply omitting to take the distributed medication [59]. To counter these unwanted effects, there is a need for people at risk to be adequately sensitised. Several studies suggest that the distribution of pre-MDA educational messages can improve compliance, such as through drug distributors who can help alleviate fear and prepare the individuals in need of treatment [53, 56, 59].

Even though funding for NTDs has increased over the past years, social sciences are still a neglected aspect of NTD control programmes, and few studies have evaluated the use of social sciences to strengthen NTD control programmes [75, 76]. As funding may be increasing, there is a need for increased interdisciplinary cooperation in order to reach the set 2020 targets [77]. The social aspects of NTD control are complex, and may be challenging to study through the use of quantitative research methods. However, studies have indicated that making use of social sciences when planning control programmes for NTDs can be highly cost-effective, and lessons learned from other infectious disease control should be integrated into current and future NTD control and elimination programmes [50].

In conclusion, social sciences, including medical anthropology, have for a long time been a neglected aspect of NTD control programmes. The results of leveraging social interventions to control emerging infectious diseases should lend inspiration to the fight against NTDs. There is a need for creative, yet robust study designs to address the challenges of quantitatively measuring relevant aspects of social sciences in a meaningful way. Qualitative

studies of other global health challenges indicate that social sciences do have an important role to play, and medical, public health and social scientists will need to find ways of working together in order to successfully combat NTDs.

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