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Review Article

An Assessment of Implications of Neglected Trypanosomiasis Disease Detection Limitations on Prevention and Control: A One Health Comprehensive Review

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Abstract

Trypanosomiasis is a Zoonotic disease which is transmitted between human beings livestock and companion animals. It is a complex and one of the notable neglected diseases of global importance. It is mainly vectored by tsetse flies, but non-tsetse insects also play a role in some cases. It claims the lives of humans, livestock and also compromises the health of companion animals hence largely affecting the livelihoods of human beings by compromising their health and food security. This paper reviewed 30 articles, looking at One Health implications of neglected Trypanosomiasis disease limitations in detection methods, on prevention and control. To come up with this paper 1,578 articles were downloaded from different data bases having peer-reviewed articles. Different phrases were used to specify the area of concentration and years were accustomed between 1990 and 2024. The study found that different techniques such as Polymerase Chain Reaction (PCR), Microscopy techniques, Card Agglutination Test for Trypanosomiasis (CATT) and Enzyme Linked Immunosorbent Assay (ELISA) are used to detect the Trypanosomes which are causative agents of Trypanosomiasis. These tools have their advantages of being sensitive and specific but are limited in that some detect only active cases and others detect only passive cases whilst others detect both. This affect reporting of prevalence in different locations and hence putting into a compromise One Health principle of informed decision making based on a reliable data set. Prevention and Control of Trypanosomiasis may either target the vector or the parasite. Methods such as the use of drugs, Trypanosomes tolerant species and traps and targets but also spraying have been reported. The different used methodologies have their strengths and weaknesses too. The problem of drug resistance has been rampant due to drug misuse and poor diagnosis of disease cases. These problems have therefore aggravated disease burden on humans, companion animals and livestock. Integration of different methodologies using One Health approach in which the triad is at the helm of prior consideration need to be advocated. Multisectoral collaboration which fosters the spirit of interdependency in dealing with zoonotic and neglected diseases but also enhanced surveillance would help to arrest Trypanosomiasis in Malawi and elsewhere on the globe. It was therefore the aim of this review to assess the implications of Trypanosomiasis disease detection limitations on prevention and control.

Keywords: *Drug Resistance; Food Security; Human Health; Multisectoral; Tsetse Flies; Zoonotic*

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Introduction

Trypanosomiasis is a general term that describes the disease existing in both humans and animals (Okello *et al*., 2015). It is a neglected zoonotic disease (WHO, 2021; WHO, 2023), which can be transmitted between human beings and other animals such as wildlife, livestock and companion animals. Trypanosomiasis primarily occur in communities where people closely associate with animals (Putri *et al*., 2023). Human African Trypanosomiasis (HAT) also called Sleeping sickness is caused by a protozoan called Trypanosoma. Acute and Chronic cases are caused by sub-species of Trypanosomes namely *Trypanosoma brucei gambiense* and *T. brucei rhodesiense* respectively (Madanitsa *et al*., 2009; WHO 2019). Apart from HAT, there also exist African Animal Trypanosomiasis (AAT) a parasitic disease of livestock and companion animals in sub-Saharan Africa. This disease kills the stated animals, hence causing tremendous losses of farm animals (Putri *et al*., 2023), and pets thereby, increasing the burden of food insecurity by compromising human livelihoods and companionship. The disease is biologically vectored by Tsetse flies but other non-tsetse biting insect vectors such as stomoxys and tabanids have been reported to mechanically transmit the disease (Okello *et al*., 2022). This hence increases the spatial and temporal existence of this disease even in the regions of non-endemism (Okello *et al*., 2022; Franco *et al*., 2020). The animal form of the disease is a very big problem for African livestock keepers and those who keep companion animals. This form has also been reported in Latin America and Asia and has potential to spread further through the globe (Boulangé *et al*., 2022). Several studies on Trypanosomiasis have been conducted but Sub-Saharan continental estimation of mean prevalence in both large and small domesticated animals including companion animals is lacking (Okello *et al*., 2015; Okello *et al*., 2022; Franco *et al*., 2020). This might be due to lack of detection tools and methodology limitations. Lack of sufficient records on risk factors, tsetse and non-tsetse prevalence and drug resistance have failed to inform prevention and control decision making at local, international even global level (Okello *et al*., 2022) hence affecting human, livestock and companion animals' health. Reports suggest that neglected tropical diseases (NTDs) harm the health and social economic development of about 1 billion people globally (WHO, 2023; Putri *et al*., 2023; Shaw *et al*., 2014). Trypanosomiasis is among the 10 Zoonotic diseases of global concern by the world health organization (WHO) (Putri *et al*., 2014). The impact of this disease might be devastating because not only does it cause human illness, but the disease also harms livestock and companion animals, thereby reducing the livelihoods of many vulnerable families by compromising their income and sources of nutrition but also the companionship rendered by the diseased pets (Putri *et al*., 2023; Okello *et al*., 2022). The danger associated with neglected parasitic diseases that revolve between humans and animals is that the role of animals in disease transmission is often overlooked (Putri *et al*., 2023). This basically emanates from the anthropocentric view that takes into account the well-being of humans more, neglecting the other important associated players that contribute much to human health. This therefore calls upon the One Health approach in neglected disease re-dress by improving detection processes and methodologies.

Several studies have been done on Trypanosome detection and Trypanosomiasis prevention and control in different regions of the globe (Putri *et al*., 2023; FAO, 1994). Despite the vast reports from the different studies and initiatives to prevent and control, there still exist upsurges of Trypanosomiasis cases (Madanitsa *et al*., 2009; Chisi *et al*., 2011; Chimera *et al*., 2021). One may tend to wonder where we have gone wrong, or if we have exhausted all the options to curb this disease. Or if we have been defeated. Studies on detection have revealed the existence of different species of Trypanosomes which cannot be dealt with by using one approach. On the other hand, several methodologies have been tried by the concerned governments, donor community and other concerned stakeholders to arrest the problem of Trypanosomiasis disease in both humans and animals. Studies have reported governments' incapacity and donor financial crippledness as notable pertinent constraints (Putri *et al*., 2023; Okello *et al*., 2022; FAO, 1994).

Beyond the stated factors, Climate change with its confounding factors have impacted on the re-emergency of not only Trypanosomiasis disease looking at the trends, but also several other infectious and non-infectious diseases (FAO, 2020a). The global disease burden (GDB) is huger than before and reports suggest that there is need to forgo traditional ways of solving disease problems and look for modern ones which are relative to present pertinent issues (Putri *et al*., 2023). In 2004 the Manhattan principles were published and came into limelight, rejuvenating the modern thinking of One Health approach (Cook *et al*., 2024). One Health is a collaborative, multisectoral, and transdisciplinary approach, working at the local, regional, national, and global levels, with the goal of achieving optimal health outcomes recognizing the interconnection between people, fauna, flora, and their shared environment (CDC, 2024). One Health championed in the Manhattan principles envisions devising adaptive, forward-looking and multidisciplinary solutions to the challenges that undoubtedly lie ahead of the 21st century human beings. Need for interdisciplinary and cross-sectoral approaches to disease prevention, surveillance, monitoring, control and mitigation but also environmental conservation has been recommended (Cook *et al*., 2024).

Integrated methodologies and approaches, such as those of One Health, are needed to address the neglected Zoonotic diseases through cross-cutting activities that involve multiple sectoral players. Effectiveness in preventing and eliminating NTDs is believed to depend on public health actions, health promotion efforts, and medical interventions (Putri *et al*., 2023), which requires multiple sectoral collaboration. One Health approach recognizes the interconnectedness of human, animal, and environmental health, and seeks to address health issues at their intersection and in an interdisciplinary manner. Implementation of One Health approaches may ensure that NTDs prevention, control and elimination efforts are sustainable and effective. Effectiveness cannot be realized if detection methods are not up to date and are not accessible by the affected individuals. This review is therefore set to assess One Health implications on neglected Trypanosomiasis disease detection limitations on prevention and control.

Methodology

The study used the literature survey approach. This methodology allows inclusion of studies conducted in different geographical regions. This allowed broader and more diverse perspective on Trypanosome detection processes and Trypanosomiasis prevalence, prevention and control limitations and their One Health implications. Different countries may have different prevention and control frameworks, practices and environmental conditions which affect the presence and distribution of vectors and Trypanosomes prevalence in their different ecosystems. By examining these studies from multiple locations, the review provides a bigger perspective on the issue under study, identifying regional differences and highlighting potential hotspots and problem areas. One thousand five hundred seventy eight (1,578) papers were downloaded from various scientific databases such as PubMed, CrossRef, AJOL and Science direct by searching keywords such as “Trypanosomiasis detection, prevention and control”, or “Trypanosomiasis Social and economic impact”, or “African Animal Trypanosomes”, or “African Human Trypanosomiasis”, or “Nagana”, or “prevalence”, or “tsetse infection”, or “biting flies” or ‘drug resistance”, or “Trypanosomes of sub-Saharan Africa”, or “Trypanosomiasis in a particular country name” were used to search for peer-reviewed articles published in the mentioned databases and later the list of papers were downloaded and abstracts critically screened and reviewed if they met the inclusion criteria (Ouzzani *et al*., 2016). Screening and selection of articles were performed according to preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) procedures (Moher *et al*., 2009) (Figure 1). This was done to ensure that appropriate articles were included in this review. Articles search was accustomed to it between 1990 and 2024. In addition, the quality of articles was also checked with considerations such as: Including articles which were published from 1990 to 2024. These are the years when tsetse eradication programs such as PATTEC have been running since their establishment in Africa (FAO *et al*., 2020). Articles mentioning; HAT or AAT, with method of diagnosis mentioned were included, those mentioning the total number of animals sampled, the species of trypanosomes causing infections, tsetse infections, biting flies associated with HAT or AAT and Trypanocidal drug resistance with species of Trypanosoma mentioned in sub-Saharan African countries were included in this review study. Articles not to mention diagnosis methods used to determine the prevalence and not mentioning the country and those mentioning tsetse flies without mentioning their infection prevalence or mentioning drug resistance without quantifying the level of drug resistance were not included.

Quality Assessment

Assessment of quality of articles was done with major considerations on; articles that were published in peer reviewed journals, studied animals and geographical locations were mentioned, appropriate sample size was mentioned and used, authentic diagnostic methods were used, accepted tsetse and non-tsetse vectors detection methods were used for assessing Trypanosoma prevalence, right trypanocidal drugs as indicated by manufacturers for use against AAT were used.

Data Extraction

Included articles were used for data extraction. Extracted data included main author and year of publication, total number of sampled humans, prevalence of HAT, total number of sampled animals, overall prevalence rate, species of Trypanosoma, diagnostic method used, species of tsetse flies, tsetse prevalence, trypanocidal drug and Trypanosoma species of resistance and prevalence of resistance.

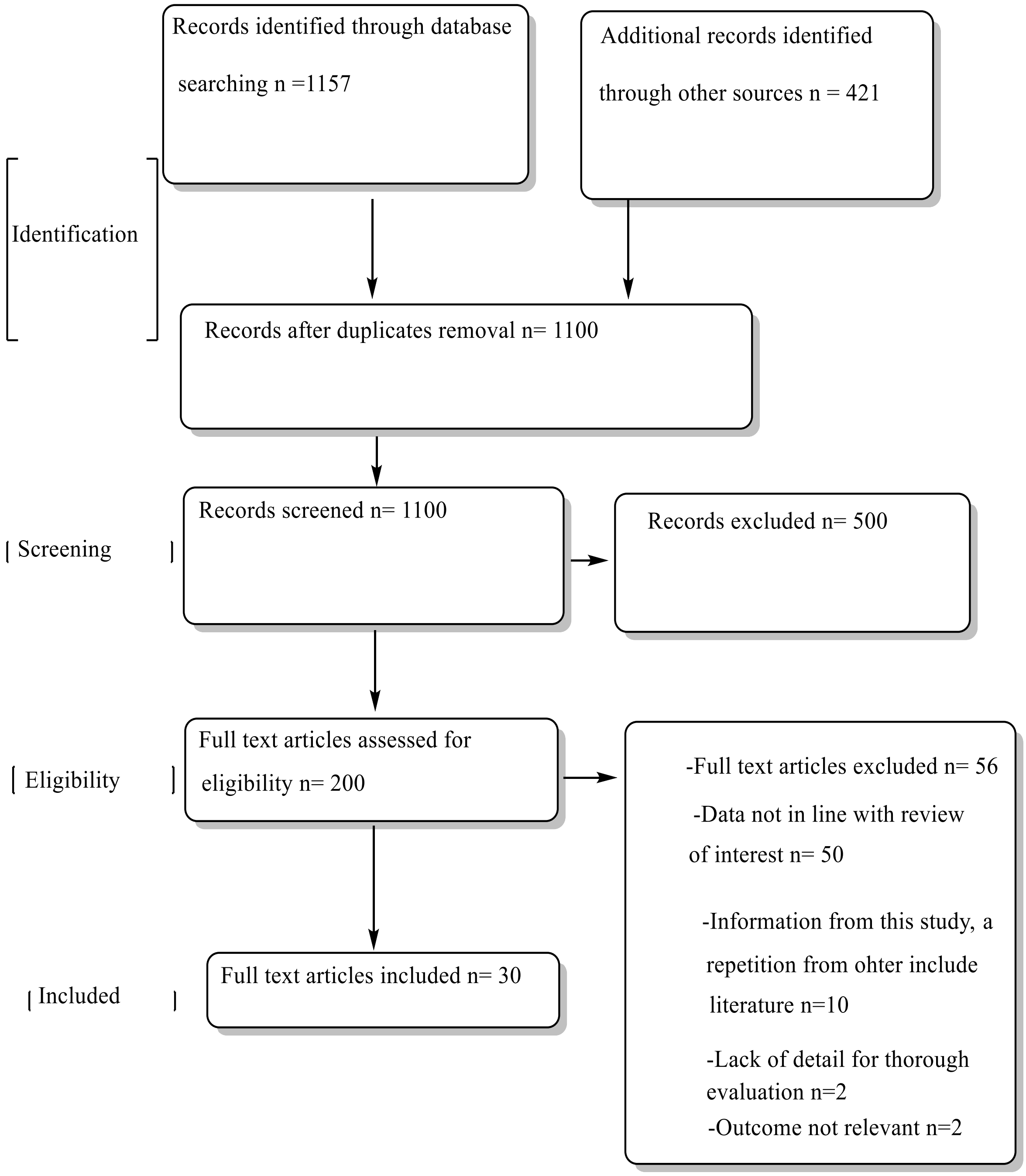

Figure 1: Showing PRISMA Process of Literature Selection

Results and Discussion

One of the major problems faced in the modern era, apart from NTDs, is sustainable agricultural production. Africa and the globe at large, need to secure adequate food production relatively more than other continents previously thought of (FAO *et al*., 2020), because of high population growth rate. In order to develop economically and at the same time feed the ever-growing population, Malawi is championing the 2063 vision with Mega farms as a component addressing maximum food productivity (Government of Malawi, 2020). Global and local food security has to be achieved amidst climate change, which has the potential of increasing the risk of emerging and re-emerging vector-borne infections (Putri *et al*., 2023; FAO, 2020a). Several vector-borne infections under NTDs do not only affect animals by reducing their biodiversity but also lowers economic benefits of livestock farmers and compromises the health of companion animals (Shaw *et al*., 2014; FAO, 2020b). In the case of Zoonoses, they can be transmitted among different animals (wild animals, livestock or companion animals) to humans and among humans as well (Putri *et al*., 2023). Cases of Covid-19, Ebola and Trypanosomiasis have cemented the understanding that globalization increases the risk of pathogens spreading fast and outside their original areas of endemicity (Franco *et al*., 2022). If disease control is to be improved, a better understanding of vector-borne infections is needed. This can only happen if proper methods of detection are in place and are accessible. Table 1 looks at some of the globally documented tsetse species, Trypanosomes commonly detected by different methods and the advantages but also limitations of these methodologies.

Diversified Vectors Associated with Trypanosomiasis disease Spread

Vector-borne African Animal Trypanosomiasis (AAT) is caused by various unicellular protozoan parasites (Trypanosoma spp.). In its different forms, AAT occurs in almost all countries in Africa. *Trypanosoma brucei, T. congolense, T. vivax* and *T. simiae* (Table 1) are transmitted cyclically (biologically) by tsetse flies (Glossina spp.), causing the disease called 'nagana' also known as sleeping sickness (Diall *et al*., 2017; OIE, 2021). *T. vivax* apart from being transmitted biologically by tsetse, can also be transmitted mechanically by other biting flies such as stable flies (Stomoxys) and horseflies (Tabanids) (Nimpaye *et al*., 2011). This behaviour has enabled the disease to be spread to other countries such as Latin America and Asia (Gonzatti *et al*., 2013; Asghari & Rassouli, 2022). These other biting flies also transmit *T. evansi*, the causative agent of 'surra', a disease that is endemic in large parts of Africa, Asia and Latin America, and also present in the Canary Islands of Spain (Aregawi *et al*., 2019). This therefore presents a need for transboundary prevention and control efforts. Surra disease problem has been reported in Europe too (Gutierrez *et al*., 2010), revealing the transboundary occurrence and its associated danger of infection, prevention and control problems. Studies suggest that increased global establishment and further spread have so far been avoided due to an effective response and reinforced surveillance in the reported areas (Desquesnes *et al*., 2009; Tamarit *et al*., 2010). This is a clear revelation that One Health principles can help in dealing with global concern because One Health emphasizes and encourages surveillance and informed decision making (Cook *et al*., 2024).

Several studies have reported that the most prevalent Trypanosoma species causing infections in most animals is *T. vivax* followed by *T. congolense* (Okello *et al*., 2022; Ngari *et al*., 2020). This is probably due to the species being able to be transmitted mechanically by non-tsetse insect vectors, which transmit the disease even in absence of biological vectors (Desquesnes & Dia, 2003). Stomoxys have been identified as the most common non-tsetse biting flies causing most infections in sub-Saharan Africa, with *Hippobosca camelina* and *Pangonia rueppellii* identified as the most common non-tsetse biting insect species in East Africa, Kenya in particular (Boulangé *et al*., 2022; Gonzatti *et al*., 2013). Eastern Africa has more reports of non-tsetse species, contributing to high prevalence of AAT cases, compared to the Western region (Desquesnes & Dia, 2003; Ravel *et al*., 2015; Abdoulmoumini *et al*., 2015). Nevertheless, tabanids, stomoxys, and other biting flies have been reported to have less impact in transmitting AAT compared to tsetse flies in sub-Saharan Africa (WHO, 2021 Ravel *et al*., 2015). This could be due to their limitation in geographical distribution (Sánchez *et al*., 2015). This knowledge is of paramount importance in the initiatives targeting eradication of the disease. It has been reported that *T. vivax* has a simple and short life cycle in which it moves from the crop of tsetse through proventriculus to proboscis hence its high prevalence in its detection (Jordan, 1974; Ooi *et al*., 2016), when detection methods that focus on proboscis of the vector compared to midgut and salivary glands are considered. Second fact is that both *T. congolense* and *T. vivax* have the widest geographical distribution (Desquesnes & Dia, 2003), hence highly encountered and detected in different studies across the globe.

In the case of domesticated animals, companion animals have been reported to be potential reservoirs for *T. brucei* sensu *lato* and *T. b. rhodesiense*, which commonly affect humans. The close association between the said animals and humans has contributed to increased chances of possible intertransmission affecting their health and the health of their masters. It has certainly been revealed that livestock and wild animals act as greater reservoirs for human-infective Trypanosomes causing Human African Trypanosomosis [HAT] (Büscher *et al*., 2018; Büscher *et al*., 2017). Being a deadly neglected tropical disease, it has been reported that over 50 million people are at risk of contracting it in twenty countries in Africa (Franco *et al*., 2020; Franco *et al*., 2022). This includes tourists and travellers in this globalized world (Simarro *et al*., 2012). One Health approach that looks at the nexus of animal, human and environmental health as an important aspect in global health is therefore important in dealing with cases of such type. Studies have also revealed that in the past twenty years, progress in AAT control has been limited due to anthropocentric view in disease control which looks at humans as most important entities and neglecting animals in disease control efforts. This is in contrast to the great strides made against HAT, which is now targeted for elimination by the World Health Organization (WHO) due to the harnessed multidisciplinary approaches (WHO, 2020).

Trypanosomiasis Diagnostic Techniques Limitations and One Health Implications

Understanding the epidemiology of Trypanosomiasis and the different species of Trypanosomes that affect the main vector thus the tsetse fly is very important, there is need to identify them accurately using methods that are very sensitive and specific (Okello *et al*., 2022). In Malawi no molecular technique had been used to identify human and animal infective Trypanosomes in tsetse flies by the year 2017 (Nambala *et al*., 2017).

Diagnostic techniques play a role in encountering differences in detection, determination and reporting of prevalence of diseases such as Trypanosomiasis. Several techniques are used in Trypanosomes detection depending on many factors such as availability and operational skills (Table 1).These techniques have their own advantages and limitations, hence one need to consider these facts when making a decision of which technique to use and how this would affect the end user on the gathered facts in decision making pertaining disease control and eradication. For instance, Polymerase Chain Reaction (PCR) tests can detect disease causing agents when there is only a very small number of pathogens in the body of an organism (Djohan *et al*., 2015). During a PCR test, a small amount of genetic material in a sample is copied multiple times. The copying process is known as amplification. If there are pathogens in the sample, amplification will make them much easier to see. PCR testing is mainly used as a confirmatory test for detecting patient parasitic infection through DNA derived from parasite stages in their developmental stages (Masiga *et al*., 1996).

Despite its reliability and widespread application, PCR technology has some limitations: PCR amplify unknown targets limiting the understanding of genome of some parasites required for disease control. Prior information about the target sequence is necessary to design the primers hence very crucial. DNA polymerases are prone to error, which potentially causes unwanted changes in PCR products. PCR is prone to producing false-negative results due to its sensitivity to inhibiting substances associated with the sample matrix and large samples are still needed if there is need to show association between different Trypanosomes and tsetse species (Masiga *et al*., 1996). A simple technique is to examine fresh blood between a coverslip and a slide with the microscope, using medium magnification (usually a dry objective of 40x or even less, and eyepieces of 5–10x). Trypanosomes are seen either directly, moving between the blood cells, or indirectly, as they cause the blood cells to move. One advantage with microscopic examination is the high sensitivity. Nevertheless, the detection limit is usually around 104 trypanosomes per ml of blood. Moreover, some species of Trypanosomes cannot be identified by utilizing the movement of the Trypanosomes in the blood sample. *T. vivax* for example, can often only be suspected if the parasites move quickly forward through the microscopical field. This can negatively impact decision making processes in One Health approach to disease prevention and control. Nevertheless, by carefully examining a thick film of parasite density, as low as 5–10 parasites/μL, in the blood worms can be detected using this microscopic technique.

ELISA is a common laboratory testing technique that detects and counts certain antibodies, antigens, proteins and hormones in bodily fluid samples. This includes blood, plasma, pee, saliva (spit) and cerebrospinal fluid (CSF). ELISA has a number of benefits compared to the other immunoassay techniques. It is often preferred because it has high sensitivity and specificity. ELISA also offers more accuracy compared to other techniques such as Radio Immune Assay (RIA) tests and PCR (Boulangé *et al*., 2022; Desquesnes *et al*., 2009). The three important limitations of an ELISA are poor repeatability, high cost, and dependence on complex equipment (Desquesnes *et al*., 2009). These would limit service access and hence increase disease economic burden. Card Agglutination Test for Trypanosomiasis (CATT) is a fast and simple agglutination test for detection of Trypanosomes' specific antibodies in blood of *Trypanosoma brucei (T.b.) gambiense* infected patients. Identification of serological suspects is the main entry point into diagnostic algorithms for g-HAT. The Card Agglutination Test for Trypanosomiasis (CATT/*T.b. gambiense*) has been the most commonly used screening test for g-HAT. It detects antibodies using a suspension of purified, fixed and stained bloodstream-form Trypanosomes expressing Lister Trypanoantigen Tag (LiTat) 1.3 variant surface glycoprotein (VSG), a predominant variant antigen of *T.b. gambiense* (Ravel *et al*., 2015). While CATT has played a central role in the control of HAT, its large-scale implementation for passive screening in health facilities in remote locations has been limited due to operational challenges such as the need for electricity and refrigeration. In some settings, the sensitivity and specificity of CATT have also been reported as being problematic (Okello *et al*., 2022), hence hindering surveillance outcomes. Despite a reported specificity of around 95%, the positive predictive value of the CATT remains limited (Birhanu *et al*., 2015; Hamill *et al*., 2013; Sokouri, 2014), this compromises tangible information dissemination which would help in decision making process.

Studies have shown differences in reported prevalence rates based on the diagnostic methods used. The use of CATT, ELISA, and PCR gave a high detection and higher prevalence rates in different host animals when compared to microscopic techniques (Mwandiringana *et al*., 2012). CATT and ELISA tests reported high prevalence probably because they detect both previous and current Trypanosome infections (Boulangé *et al*., 2022). On the other hand, molecular PCR also showed higher prevalence because, it is a method that has been confirmed to have a high detection rate in both acute and chronic stages of AAT (Desquesnes, 1997). It is very sensitive and specific hence highly and worldly used in Trypanosome detection (Djohan *et al*., 2015). On the contrary, some studies have reported lower prevalence in PCR due to the fact that they detect only fresh infections (Ravel *et al*., 2015). Using less sensitive diagnosis techniques may have given a limited indication of the prevalence rates in some of the studies that have been previously reported. This may have led to poor decision-making in handling some of the disease cases.

Animal Trypanosomiasis still kills and reduces the productivity of millions of cattle. Economic losses encountered by livestock producers due to AAT are huge, with further losses occurring within the agricultural sector due to climate change impact (Shaw *et al*., 2017). There are many reasons why AAT continues to afflict African livestock producers and continue to lower food security (Diall *et al*., 2017). One notable problem is the neglect of the disease but also climate change impact which requires multisectoral address. One cannot refute the necessity of multidisciplinary collaboration in dealing with Trypanosomiasis. Looking at the complexity of disease, which has several species of hosts, parasites, vectors, and reservoirs in wildlife, livestock but also companion animals, the need for collaboration of all responsible stakeholders is greater now than then. Largely AAT and HAT control is hindered by poor surveillance mechanisms, scanty data of the disease impact socio-economically, and poor planning in prevention and control initiatives. In addition, farmers and veterinary services have limited access to modern technologies, and when technology is available, they often lack the expertise to apply it effectively. One crucial fact is that most affected countries are developing countries, with limited resources to control disease cases. One Health approaches of collaboration and information dissemination would therefore greatly help in prevention and control of NTDs such as Trypanosomiasis.

Table 1: Showing Different Tsetse Species, Trypanosomes and Different Detection Methods and Their Limitations

Tsetse Species	Trypanosome Type	Diagonostic Technique	Advantages	Disadvantage/Limitation
G. nigrofusca	*T. brucei gambiense*	PCR	Very sensitive/active detection	Expensive/Requires skills
G. palpalis	*T. congolese kilifi*	ELISA	Sensitive	Expensive/ Indicate past &present contacts
G. swynnertoni	*T. congolese forest*	CATT	Sensitive	Expensive/ Indicate past &present contacts
G. longipenennis	*T. congolese savanna*	MICROSCOPY	Relatively cheaper	Less sensitive compared to PCR, ELISA, CATT
G. tachinoides	*T. evansi*			
G. morsitans	*T. simiae*			
G. pallicera	*T. vivax*			
G.pallipides	*T.godfreyi*			
G. migrofusce	*T. brucei rhodesiense*			
G. fuscipes	*T. congolese kenya*			
	T. theileri			

Trypanosomiasis Prevalence, Drug Resistance and Need for Improved Accessible Detection Techniques

Studies have reported high prevalence of Trypanosomiasis in both animals (AAT) and humans (HAT). Studies suggest high drug resistance associated (Geerts *et al*., 2001; Kulohoma *et al*., 2020), with high AAT prevalence in cattle, goats, and sheep in countries such as Ethiopia, Equatorial Guinea and Nigeria (Table 2). On the other hand, countries like, Gabon and Senegal reported no cases of drug resistance with the lowest AAT prevalence in host animals (Okello *et al*., 2022). This shows that among other factors, drug resistance could indeed contribute to increasing AAT and HAT reported cases. A similar association has been reported in Burkina Faso (McDermott *et al*., 2003). Solomon and Workineh (2018), suggested that high levels of AAT prevalence over the past years could be attributed to increasing drug-resistant Trypanosomes, lack of consistency in control strategies and programs (Adungo *et al*., 2020) and poor use of trypanocidal drugs (Dagnachew *et al*., 2017), among others. *T. congolense* followed by *T. vivax* have been documented as more resistant to trypanocidal drugs possibly because they are more diverse and pathogenic species (Tchamdja *et al*., 2017). This might be the reason for their high prevalence in many reported studies (Okello *et al*., 2022; Ngari *et al*., 2020; Nimpaye *et al*., 2011; Masiga *et al*., 1996). Additionally, studies have reported increasing incidence of drug-resistant species with *T. Congolense* being the most resistant and most prevalent (Okello *et al*., 2022; Nimpaye *et al*., 2011; Masiga *et al*., 1996). The diversity brought about by drug resistance species requires improved and accessible detection mechanisms and technologies. There is therefore high need to consider these present limitations in targeted disease control initiatives, such as those of One Health to effectively and efficiently prevent and control Trypanosomiasis disease.

Table 2: Reported Trypanosoma Species and Drug Name

Country	Trypanosoma Species	Drug Name	Reference
Ethiopia	*T. congolense*	Diminazene	Afewerk *et al*., 2000; Assefa and Abebe, 2018
	T. vivax		Moti *et al*., 2012; Dagnachew *et al*., 2015, 2017b; Mekonnen *et al*., 2018; Degneh *et al*., 2019; Tadele *et al*., 2019
Ethiopia	*T. congolense*	Isometamidium	

	T. vivax		Afewerk *et al*., 2000; Assefa and Abebe, 2018; Moti *et al*., 2012; Dagnachew *et al*., 2015, 2017b; Degneh *et al*., 2019; Tadele *et al*. 2019
Kenya	*T. congolense* *T. brucei*	Diminazene	Mugunieri and Murilla, 2003; Mapenay and Maichamo, 2008; Ndung'u *et al*., 2020 and Maichamo, 2008; Ndung'u *et al*., 2020
Kenya	*T. congolense*	Isometamidium	Mugunieri and Murilla, 2003; Mapenay and Maichamo, 2008
Mozambique	*T. congolense*	Diminazene	Jamal *et al*., 2005; Mulandane *et al*., 2018
Mali	*T. congolense*	Diminazene	Talaki *et al*., 2006; Mungube *et al*., 2012
Mali	*T. congolense*	Isometamidium	Talaki *et al*., 2006; Mungube *et al*., 2012
Mali	*T. vivax*	Isometamidium	Talaki *et al*., 2006; Mungube *et al*., 2012
Nigeria	*T. congolense*	Diminazene	Anene *et al*., 2006; Odeniran *et al*., 2019
Nigeria	*T. vivax*	Diminazene	Anene *et al*., 2006; Odeniran *et al*., 2019
Burkina Faso	*T. congolense*	Diminazene	Chitanga *et al*., 2011; Vitouley *et al*., 2011
Burkina Faso	*T. vivax*	Diminazene	Chitanga *et al*., 2011; Vitouley *et al*., 2011
Cameroon	*T. brucei*	Diminazene	Mamoudou *et al*., 2008
Cameroon	*T. congolense*	Isometamidium	Mamoudou *et al*., 2008
Cameroon	*T. brucei*	Isometamidium	Mamoudou *et al*., 2008
Togo	*T. congolense*	Isometamidium	Tchamdja *et al*., 2017
Togo	*T. vivax*	Isometamidium	Tchamdja *et al*., 2017
Tanzania	*T. brucei*	Diminazene	Kibona *et al*., 2006
Equatorial Guinea	*T. congolense*	Diminazene	Talaki *et al*., 2006
Equatorial Guinea	*T. vivax*	Isometamidium	Talaki *et al*., 2006
Zambia	*T. congolense*	Diminazene	Sinyangwe *et al*., 2004, Delespaux *et al*., 2008
Zambia	*T. vivax*	Diminazene	Sinyangwe *et al*., 2004, Delespaux *et al*., 2008
Zambia	*T. brucei*	Diminazene	Sinyangwe *et al*., 2004, Delespaux *et al*., 2008
Zambia	*T. congolense*	Isometamidium	Sinyangwe *et al*., 2004
Zambia	*T. vivax*	Isometamidium	Sinyangwe *et al*., 2004
Zambia	*T. brucei*	Isometamidium	Sinyangwe *et al*., 2004

Need for Multisectoral Approach Enhancement

Upsurges of HAT and AAT in some parts of Africa, Malawi inclusive (Madanitsa *et al*., 2009; Chisi *et al*., 2011; Chimera *et al*., 2021) and also globally (WHO, 2019), have been reported. To ease the economic cost of Trypanosomiasis disease burden, there is need for national and inter-country identification of prevalent species, disease incidences and genetic variation of drug-resistant species using standard molecular techniques which are also accessible by majority poor individuals in developing countries. It will be highly beneficial to identify the true prevalence of AAT and HAT, identify the presence of drug-resistant species which will help improve governments' policies on the use of drugs, and also give an indication of transmission of drug-resistant Trypanosoma species across countries. Sensitizing livestock and companion animals keepers', under information dissemination as stipulated in One Health approach strategies, will help control and reduce the spread of Trypanosomiasis. Giving more research attention to better understand and control AAT and HAT by means of informed decisions making would help achieve One Health and global health with ease. Many different prevention and control techniques have been applied in different situations encountered at local and global level (FAO, 1994). Some have worked and others have not. Harnessing enhanced One Health approaches is therefore handy looking at the complexity of Trypanosomiasis disease which has been neglected for long and has affected the livelihoods of masses in Africa and Malawi in particular (WHO, 2021). Many individuals in developing countries who are already vulnerable to lots of unforeseeable calamities such as covid -19 and cyclones have been affected, hence having reassessment of the methodologies that have been applied in different countries is of paramount importance. Incorporation of One Health principles would be handy in this era of globalization. Table 3 outlines some of the most common methods that have been tried to control Trypanosomiasis and their limitations as a common global stand.

There are different strategies that are in use for Trypanosomiasis prevention and control. Although very advantageous in many ways they are not completely without limitations. Some are well recommended and others not (Table 3). The approach to Trypanosomiasis prevention and control can be looked at in two phases. One may consider controlling the parasites while others may target the vectors (Allsopp, 2001).

Parasite Control

Parasites are controlled using drugs. Drug therapy has been in the past the main control method of Trypanosomiasis in many different countries. Although this has been effective, there has been one big problem of drug resistance (Okello *et al.,* 20522) due to drug mismanagement (Geerts *et al*., 2001; Kulohoma *et al*., 2020). Lack of reliable information on the true extent of Trypanosomiasis problem as previously highlighted has contributed to poor planning of national education campaigns for its eradication. Drug supplies due to poverty in many African countries are usually scanty exacerbating the problem to a higher level. A blame has been thrown also on some movements in some countries where the Trypanocidal drug distribution and sales are left in the hands of the private sector who their core purpose is profit making. This compromises the health of humans, livestock but also companion animals. Studies have recommended that drug prophylaxis should only be considered where a proper drug management system can be established and maintained (FAO, 1994).

Trypanotolerant Livestock

Studies have shown that although most indigenous livestock breeds exhibit a degree of Trypanosome tolerance when compared to the exotics, it must be accepted that these animals are susceptible to Trypanosomiasis under high challenge or physiological stress, caused by poor drought conditions (FAO, 1994). The tolerant trait is particularly pronounced in the N'Dama and West African Shorthorn stocks of West and Central Africa (Okello *et al*., 2022) which are probably unsuited to the more arid conditions. Also where the priorities are for high milk production and other functionalities such as draught animals, owners strongly prefer other breeds such as Zebu, which are more susceptible to Trypanosomiasis. This preference overrides the initiatives to prevent and control Trypanosomiasis through use of Trypanosomiasis tolerant species of livestock. It is very crucial and unrealistic due to individual farmers' preference and reasons (FAO, 1994). There is therefore need to balance farmer's preference of high production and the need to prevent and control Trypanosomiasis disease.

Vector Control

Ground Spraying

Spraying has been a debatable method of controlling tsetse due to its use of Dichloro-diphenyl-trichloroethane (DDT). DDT usage was highly questioned in 1962 after Rachel Carson published her book titled the 'Silent springs'. 'Silent Spring' is an environmental science book that documented the environmental harm caused by the indiscriminate use of DDT. Spraying was seen as a tool to achieve localized eradication. Occasionally ground spraying was used as a control method to reduce fly challenge in human sleeping sickness endemic areas (FAO, 1994). In recent years, the use of ground spraying has declined to very minimal levels, for a variety of reasons such as, global environmental pressures against the use of DDT, development of more environmentally acceptable chemicals, and use of simpler and cheaper methods such as tsetse traps and targets (Abdoulmoumini *et al*., 2015; Geerts *et al*., 2001).

Reports suggest that this ground spraying technique remains a suitable option for eradication of morsitans and palpalis flies (FAO, 1994). Although others argue that it is not suitable for community-based programmes because it requires technical supervision which is costly to implement (Boulangé *et al*., 2022; FAO, 1994).

Aerial Spraying

It is a spraying method that involves applying a single residual deposit of a persistent insecticide to the more restricted, dry season habitat of the fly. It targets the riparian vegetation, using the helicopter downdraught to force the insecticide through the upper canopy (FAO, 1994). The technique is more costly, and the side-effects on non-target organisms are acute and long lasting because of the used persistent organic pollutants (POPs) in the insecticides (Geerts *et al*., 2001; Kulohoma *et al*., 2020). It is reported that this technique was used in the past in West Africa in programmes to eradicate the Palpalis and Morsitans groups of flies from the savanna and guinea zones of Nigeria and is still operational against *G.m. submorsitans* in the highlands of Adamoua in Cameroon (Abdoulmoumini *et al*., 2015; Geerts *et al*., 2001). Its one main advantage is that large areas could be effectively and quickly treated hence reducing cost but the fear is it could compromise biodiversity in the environment (FAO, 1994).

Sequential Aerosol Spraying

This involves the use of fixed-wing aircraft applying a sequence of 5 or 6 applications at 12–20 day intervals of extremely low dosage, non-residual, insecticide as a fine aerosol. It is in records that it was extensively used over the last 25 years in eradication programmes against the Morsitans group of flies in the savanna locations of southern and eastern Africa and reports suggest that it has also been used against the Palpalis group in West Africa (FAO, 1994; Abdoulmoumini *et al*., 2015). Its main advantage is that large areas can be treated with little or no reliance on ground workers. And off-target side-effects are comparatively minimal when compared to aerial spraying. Studies suggest that it can be used in rapid treatment of large areas in human sleeping sickness epidemics, where there is an urgent requirement for vector population reduction (FAO, 1994).

Sterile Insect Technique (SIT)

The sterile insect technique (SIT) is among the most environment-friendly insect pest control methods ever developed. Irradiation, such as with gamma rays and X-rays, is used to sterilize mass-reared insects so that, while they remain sexually competitive, they cannot produce offsprings. This technique is only justifiable if the objective is eradication and it can be achieved at reasonable cost. It is species-specific and non-contaminating to nature (FAO, 1994).

Traps and Targets

Traps are very effective at countering insects. These can target certain species without harming the ecology of an area. These can be preventative or employed solely for insect outbreaks. Traps or toxic targets are visual and olfactory baits. The basic trapping principle is to attract insects that are looking for a host, using visual and possibly olfactory lures to lead them inside traps, either to keep them alive using a capture system, or to kill them with an insecticide. Recent development of relatively efficient traps and targets, enhanced with attractive odors, has opened up considerable possibilities for the control of many tsetse species (Desquesnes *et al*., 2021). The limitation is that some species such as the Palpalis group is much less responsive to the range of synthetic odours developed than is the Morsitans group (FAO, 1994). Nevertheless, the method has been applied in countries like Côte d'Ivoire, mainly against the riverine species, *G. palpalis* and *G. tachinoides* (Okello *et al*., 2022; FAO, 1994, Djohan *et al*., 2015).

Insecticide Treated Livestock (ITL)

ITL involves treating livestock living in close proximity to humans with an insecticide. This technique can also be applied to companion animals to prevent them from biting vectors. Zoophagic Trypanosomiasis vectors may die or have reduced reproductive success hence protecting humans, livestock and companion animals from disease transmission (Okello *et al*., 2022). ITL is a modified technology of the target method whereby, instead of stationary traps, animals are treated with insecticides. The insecticides are applied by dipping or the use of individual "pour-on" applications. The dipping of cattle, combined with the use of "pour-on" in areas of *G. pallidipes* and *G. morsitans* infestations has led to a very high degree of vector suppression and Trypanosomiasis control (FAO, 1994). In some countries such as Zimbabwe and Burkina Faso, where there is no dipping infrastructure and drug supply is rare, this method might prove to be effective (Adungo *et al.*, 2020).

Table 3: Showing the Different Prevention and Control Strategies of Trypanosomiasis

Strategies	**Limitations of the Strategies**
Parasite Control	
Use of drugs	Drug resistance
Trypanotolerant Livestock	Susceptibility when stressed
Trypanotolerant Livestock	Low productivity
Vector Control	
Spraying (ground, aerial)	Environmental pollution
Sterile Insect Technique (SIT)	Infringement to natural processes
Traps and Targets	Environmental pollution
Insecticide Treated Livestock	Environmental pollution

Conclusion

Trypanosomiasis affects a lot of animals and humans, hence impacting livelihoods and health. This disease is capable of causing disabilities and to a large extent fetal. Eradication seems to be a problem due to a number of factors such as lack of implementation and limitations of detection methods, prevention and control efforts are compromised due to limited access to appropriate diagnostic equipment and lack of community engagement in prevention and control strategies. Lack of coordination but also collaboration among different stakeholders and lack of political will by many governments. One Health approaches such as improved surveillance, informed decision making through proper diagnostic tools, and multisectoral collaboration in drug administration processes are far reached and this makes Trypanosomiasis disease eradication to remain a problem. It is therefore plausible that before indulging in a control campaign, epidemiological surveys should be done using appropriate diagnostic techniques in order to ascertain the degree of the problem. This would help to reduce cases of drug resistance as observed in cases where mass drug administration was recommended without proper guidance. Detection tools should be informative to enable proper decision making, prevention and control methods of Trypanosomiasis should be environmentally friendly to avoid loss of biodiversity through pollution and degradation of the environment. All stakeholders need to take their part. Collaboration in all initiatives concerning NTDs such as Trypanosomiasis is of paramount importance. In practice, there are many different situations in Trypanosomiasis disease handling. These require different methods, and integrated approach is necessary. This can mean using different techniques in adjacent areas or using two or more overlaid techniques in the same area. To achieve a greater goal in Trypanosomiasis eradication campaigns, enhanced One Health approach with situation analysis and systems thinking taking a centre stage is a way to go.

CRediT Authorship Contribution Statement

James Majamanda: Conceptualization, Methodology, writing and editing. Andrew Mtewa: Supervision, review, writing and editing. Mwayiwawo Madanitsa: Supervision, review & editing. Steven Gowelo: Supervision, review and editing.

Instruction for AI Assistance Declaration

The author hereby declares that, during the preparation of this manuscript, generative AI tools such as ChatGPT, Microsoft Copilot, and Google Gemini were utilized to assist with language enhancement and grammar correction. Following the use of these tools, the author thoroughly reviewed and revised the content and takes full responsibility for the final version of the manuscript, ensuring its accuracy and adherence to the required academic standards.

Conflict of Interest

The authors declare that there is no conflict of interest as the research was not conducted for commercial or financial purposes.

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