FACULTY OF VETERINARY MEDICINE
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Evaluating One Health – CYSTISTOP case study

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Preface

What should have been a fantastic final year and a huge experience with research that I could carry out in Zambia, turned out differently. Unfortunately, COVID19 threw a spanner in the works, not only for me, but also for my fellow student Sophie and for the whole project itself. Nonetheless, I really enjoyed this final year and carried out this research with great pleasure. A big thank you to Professor Gabriël and Dr. Trevisan for welcoming me so warmly and giving me the opportunity to initially go to Zambia and be part of the project in some way. In the beginning, conducting the study was difficult because there was still a lot to learn. But thanks to your feedback, good help and especially patience, I made it this far. Also, a big thank you to everyone who participated in the interviews, it was a pleasure, and your enthusiasm was great!

Thank you so much!

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List of Abbreviations

AMR: Antimicrobial Resistance
ASF: African Swine Fever
BCE: Before the Common Era
COVID19: Coronavirus disease of 2019
DALY: Disability-Adjusted Life Year
EITB: Enzyme-linked immunoelectrotransfer blot
ELISA: Enzyme linked immunosorbent assay
EU: European Union
FAO: Food and Agriculture Organization of the United Nations
NEOH: Network for Evaluation of One Health
OH: One Health
OHI: One Health index
OHR: One Health Ratio
OIE: World Organisation for Animal Health
SSA: sub-Saharan Africa
TOC: Theory of Change
WHO: World Health Organization

Summary

The One Health approach is leading in finding solutions for today's complex health problems. Essential to this approach is addressing a health problem by including different disciplines and sectors with the common goal to achieve health for humans, animals and the environment. Especially, tackling zoonotic diseases requires a multidisciplinary collaboration foreseen in the One Health approach. This also applies to the zoonotic parasite *Taenia solium* as it is responsible for an enormous burden on human health and animal health, especially in developing countries. CYSTISTOP, a seven-year *T. solium* control project conducted in the Eastern Province of Zambia, aims to find sustainable control and/or elimination measures applicable in sub-Saharan African conditions. Controlling and or eliminating the parasite requires sustainable measures, making an integrated and multidisciplinary One Health approach indispensable. Conducting a One Health evaluation provides feedback on how One Health is implemented in a project and demonstrates its strengths and weaknesses. In this study, the implementation of One Health in CYSTISTOP was assessed according to the evaluation framework developed by the Network for evaluation of One Health. This evaluation assesses 4 essential elements namely (1) the description of the initiative and its context, (2) the description of the initiatives Theory of Change with identification of essential building blocks, (3) a quantitative assessment of the 'One Healthness' and (4) an assessment of the outcomes of the initiative in relation to the results obtained in element 3. To conduct this evaluation, available literature, the CYSTISTOP protocol and questionnaires were used. Outcomes of this study showed that CYSTISTOP is a well-balanced initiative regarding supporting and operational aspects, obtaining a One Health ratio of 0,97. The integration of One Health, represented as the One Health Index, is 0,78. Interdisciplinary teamwork, data sharing and systemic organisation are in this project along with feedback and joint decision making. Although not all results of CYSTISTOP are available yet, its outcomes have provided valuable information in *T. solium* research in sub-Saharan Africa and paved the way for future interventions. In order to be able to implement measures, to tackle *T. solium*, on a larger scale, stakeholders at higher levels should be involved and greater emphasis should be placed on environmental health.

Keywords: One Health – Network for evaluation of One Health – One Healthness – CYSTISTOP – *Taenia solium* – taeniosis

Samenvatting

De ‘One Health’ benadering is toonaangevend bij het vinden van strategieën voor de complexe hedendaagse gezondheidsproblemen. Essentieel bij deze aanpak is dat deze gezondheidsproblemen aangepakt worden vanuit de samenwerking tussen verschillende disciplines met als gemeenschappelijke doel gezondheid voor mens, dier en milieu. Ook bij het vinden van maatregelen voor het beheersen van zoönosen is een multidisciplinaire samenwerking essentieel. *T. solium,* een zoönose, is verantwoordelijk voor een aanzienlijke gezondheidslast voor mens en dier, voornamelijk in ontwikkelingslanden. CYSTISTOP, een 7 jaar durend project uitgevoerd in de oostelijke provincie van Zambia, werd opgericht met als doel het vinden van duurzame bestrijdings- en/of controlemaatregelen. Hierbij is een One Health aanpak onontbeerlijk. Desalniettemin is het uitvoeren van een One Health evaluatie noodzakelijk, het geeft feedback over de implementatie van One Health binnen een project en toont de sterktes en zwaktes. In deze studie wordt de implementatie van One Health binnen het CYSTISTOP-project beoordeeld volgens het evaluatiekader dat door het ‘Network for Evaluation of One Health’ ontwikkeld is. In deze evaluatie worden 4 essentiële elementen beoordeeld, namelijk (1) de beschrijving van het initiatief en zijn context (2) de beschrijving van de veranderingstheorie met de identificatie van het project haar essentiële bouwstenen, (3) een kwantitatieve beoordeling van de "One Healthness" en (4) een beoordeling van de uitkomsten van het initiatief in relatie tot de in element 3 verkregen resultaten met het formuleren van aanbevelingen. Voor het uitvoeren van deze evaluatie werd gebruik gemaakt van beschikbare literatuur, het CYSTISTOP-protocol en vragenlijsten. Uit de resultaten van deze studie blijkt dat CYSTISTOP een evenwichtig initiatief is wat de ondersteunende en operationele aspecten betreft, waarbij de One Health ratio 0,97 bedraagt. De integratie van One Health, weergegeven als de One Health index, bedraagt 0,78. Interdisciplinair teamwork, het delen van gegevens en systemische organisatie zijn binnen dit project grote troeven gebleken, samen met feedback en gezamenlijke besluitvorming tussen de betrokken disciplines. Ondanks het feit dat nog niet alle resultaten van CYSTISTOP’s interventiestudies bekend zijn, hebben de uitkomsten reeds waardevolle informatie opgeleverd voor andere studies en toekomstige interventies. Echter, om maatregelen ter bestrijding van *T. solium* op grotere schaal te kunnen uitvoeren, worden idealiter belanghebbenden op hogere niveaus bij het project betrokken en moet meer nadruk worden gelegd op het omgevingsaspect.

Kernwoorden: One Health – Network for evaluation of One Health – One Healthness – CYSTISTOP – *Taenia solium* – taeniosis

1. Literature review

1.1 One Health

1.1.1 Introduction: The establishment of the term 'One Health'

In the 21st century, global society suffered from several emerging zoonotic diseases, including severe acute respiratory syndrome, bovine spongiform encephalopathy and the outbreak of the highly virulent avian influenza strain, all of which had major impact on humanity (Gibbs, 2005). As a direct response to these global health threats, governments and scientists agreed that these rapidly emerging zoonotic diseases had to be approached via integrated measures to prevent future worse ones. Where in previous years only veterinarians and physicians would be involved, this integrated approach to address zoonoses and other health threats now included additionally experts in the fields of economy, humanity, sociology and the environment. This concept which uses an integrated approach regarding different disciplines and sectors, and recognises the commonality between human, animal and environmental health was from then on presented as the 'One Health' (OH) concept (Gibbs, 2014).

In 2004, the Wildlife Conservation Society organised a conference to stress the importance of the link between wildlife disease, ecology and zoonotic diseases. During this conference, the term 'One world - One health' was introduced, embracing the common view on human and animal medicine as well as environmental health. In addition, the 'Manhattan Principles' were presented, a list consisting of 12 recommendations to enable a holistic and integrated approach towards endemic and zoonotic diseases and to preserve the integrity of the ecosystem. From here, the OH concept evolved further, gaining worldwide recognition and acceptance on a large scale by veterinarians and agencies responsible for the control of zoonotic diseases i.e. the World Health Organisation (WHO), Food and Agriculture Organisation (FAO) and the World Organisation for Animal Health (OIE) (Gibbs, 2014).

1.1.2 Recognition of One Health before the 21st century

The idea of interdependent health has been circulating among mankind for a very long time, precisely because health itself is a basic requirement for life on earth. Throughout history of mankind, the concept of OH has been studied and elaborated on further. The connection between humans, animals and the environment has been central to many cultures and in spiritual attitudes for centuries, and even in contemporary aboriginal civilizations. The Greek physician Hippocrates addressed the OH concept in his book 'Airs, Waters and Places', written in the 5th or 4th century Before The common Era (BCE). In these writings he conceptualised the influence of the environment in occurring human disease (Evans and Leighton, 2014).[1]

The link (but not the understanding about physiology) between proximity to swamps (an environmental factor) and getting malaria had already been established around 400/500 BCE, although it was first written about in the 17th century by the Italian physician, epidemiologist and veterinarian Giovanni Maria Lancisi. Besides describing the importance of the environment in spreading disease between humans and animals, Giovanni Maria Lancisi is the pioneer in tackling the rinderpest using various strategies such as reducing population density of cattle, using quarantine measures as well as draining marshes as a protection measure. Additionally, protection was used against biting flies and mosquitoes for malaria prevention. This shows that it has been known for a long time that there is a correlation between human, animal and environmental health (Evans and Leighton, 2014).[1]

Physicians studied comparative anatomy and performed experiments and surgical procedures on live animals and later took interest in animal health long before the veterinary profession was found (Henrique Franco, 2013). The London veterinary College, founded in 1791, was founded and run mainly by physicians dedicated to the study of animals (Woods and Bresalier, 2014). Awareness continued to

[1] https://www.britannica.com/topic/public-health#ref412417 (Last consulted March 2021)

evolve, as the German physician Rudolf Virchow (1821-1902) stated the following words: 'Between animal and human medicines there are no dividing lines – nor should there be. The object is different, but the experience obtained constitutes the basis of all medicine'. Virchow created the term zoonosis to designate human illness caused by animal diseases. In addition, Virchow recognised the importance of the environment for health outcomes and emphasised that human and animal health as well as diseased did not differ in kind, but only in detail (Evans and Leighton, 2014; Greek, 2012).

1.1.3 The fundamentals of a One Health approach

The fundamental idea of a OH approach is to achieve overall health at the human-animal-environmental interface through a collaborative, multisectoral and multidisciplinary approach at local, regional, national and global levels (Ryu et al., 2017). As illustrated in Figure 1, coordination, communication and collaboration between human, animal and environmental partners are key in this concept.

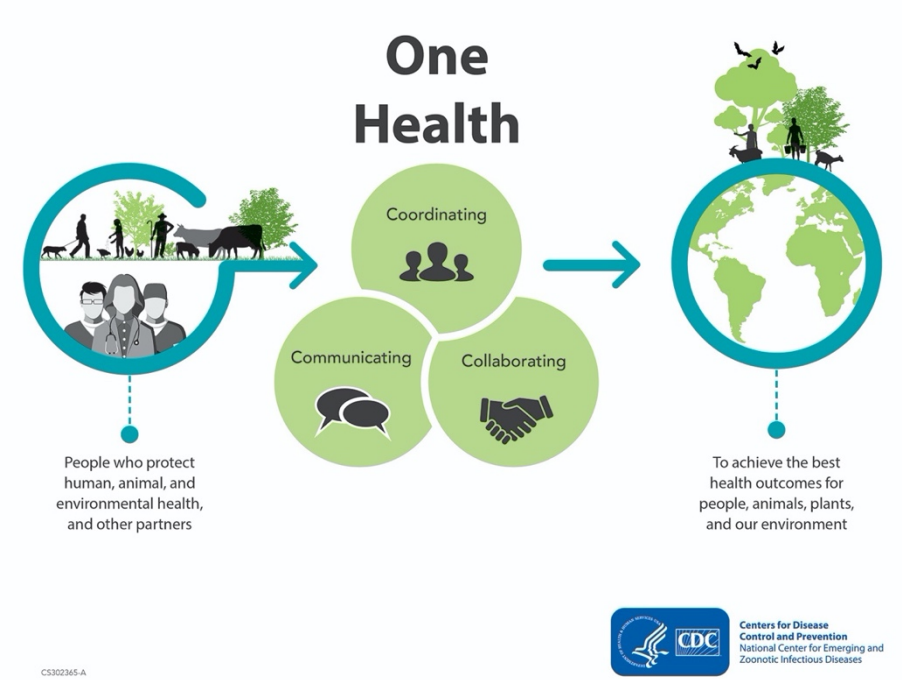

Figure 1. The backbone of a One Health approach relies on communication, coordination and collaboration (CDC, 2019)

1.1.3.1 A collaborative multisectoral and multidisciplinary approach

Health provision and research have traditionally been divided into areas of human, animal and environmental health. As knowledge of the need for collaborative approaches with regard to zoonotic diseases increased, the OH concept enabled different sectors to actually work together (Rüegg et al., 2018a). For instance, in 2010, the FAO, OIE and WHO established the FAO-WHO-OIE tripartite. This collaboration has stated the following vision: 'A world capable of preventing, detecting, containing, eliminating, and responding to animal and public health risks attributable to zoonoses and animal diseases with an impact on food security through multi-sectoral cooperation and strong partnerships' (WHO-FAO-OIE, 2010). This tripartite, working at the human-animal-ecosystem interface illustrates that cooperation is feasible. Combining these sectors, each with their specified expertise, leads to a worldwide health security system through these organizations individually and their cooperation (WHO-FAO-OIE, 2010). In addition, the WHO, FAO and OIE signed a memorandum in 2018, declaring that these organisations agree to work together closely in the long term to address health hazards at the human-animal-ecosystem interface.[2] This shows that the OH approach facilitates partnerships and

[2] https://www.who.int/zoonoses/concept-note/en/ (Last consulted March 2021)

cooperation between organisations with different objectives and conflicts of interest (van Herten et al., 2019).

1.1.3.2 A mission on local, regional, national, international and global level

The tripartite operates at global level, however OH efforts must additionally be made at national, regional and local level. Many countries have already invested in this approach. The Belgian institute Sciensano can be taken as an example. Sciensano is a product of the merge of two institutes with both more than 100 years of field experience namely, the Scientific Institute of Public Health (ISP), addressing public health and the Veterinary and Agrochemical Research Centre (CERVA) addressing research in veterinary sciences and agrochemistry. This merge complements the OH approach with its multidisciplinary collaboration, investing in animal health, effectiveness and safety of vaccines, food consumption and food safety, health and disease monitoring, health and environment and quality of healthcare. In addition, Sciensano is active at regional, federal, community, European and international levels.[3]

1.1.3.3 One Health and the Three pillars of sustainability

The Three Pillars of Sustainability refer to the harmony between economic balance, environmental protection and social equity, 3 aspects needed for to achieve sustainable development (Purvis et al., 2019). The OH approach shows parallels to this concept of sustainability as these factors all are inherent to a OH approach since sustainable development can only be achieved when cooperation takes place within these 3 systems (Purvis et al., 2019; Rüegg et al., 2018a)

As described in the previous sections, environmental health and protection is a vital part of the OH approach. In addition, the OH approach includes the economic sector which will be further demonstrated in section 1.1.4 'benefits of a OH approach'. OH interventions additionally take various social factors into account e.g. the investigation of local acceptability, maintaining solidarity, and supporting equality and diversity (Rüegg et al., 2017).

1.1.3.4 Health objectives

Health for humans, animals and the environment is a broad concept, and therefore does not only include emerging infectious and zoonotic diseases. As the OH approach evolves, other topics became relevant to this approach, which was not the case when the OH concept was first proposed. These topics contribute to health in the broader context and include contemporary non-infectious diseases including multifactorial and chronic diseases e.g. cardiovascular disease, cancer, metabolic disorders in humans and animals, sanitation, vector control, disease surveillance, research of vaccines and therapeutics, biological hazards and pollution, antimicrobial resistance (AMR), food safety and -security and mental wellbeing (Gibbs, 2014).[4]

1.1.4 Benefits of a One Health approach

1.1.4.1 Efficiency in surveillance and disease management

The implementation of a OH approach is ought to improve efficiency throughout different sectors, locally, nationally and potentially internationally. The result is a more efficient communication, which generates a higher degree of awareness leading to a more rapid problem detection and adequate action (Rüegg et al., 2019). Additionally, with deployment of OH on large scale, it is ultimately expected that the health of humans, animals and the ecosystem will jointly be managed by common health strategies (Rüegg et al., 2018a).

[3] https://www.sciensano.be/en/about-sciensano/history-sciensano (Last consulted March 2021)
[4] https://onehealthinitiative.com/about/ (Last consulted March 2021)

Health surveillance systems are a critical factor to prevent, monitor and manage disease and to enable rapid detection and intervention (George et al., 2020). In the last 2 decades, increasing efforts have been made to integrate the health surveillance system in different ways, from the integration of data sources to changing organisational structures. This integration, stemming from the OH concept, has proven highly beneficial due to the growing demand for joint data collection and - use, and awareness of emerging infectious diseases (George et al., 2020).

Unfortunately, there are many examples of situations where health surveillance could be improved, showing that a OH approach could have prevented the spread of disease outbreak. For instance, public and animal health surveillance systems do often not completely succeed in communicating together, resulting in devastating effects on health. An outbreak of Q-fever in the Netherlands (2007-2010) can be taken as a vivid example of how a difficult cooperation between those two sectors has led to extensive problems (Enserink, 2010). Lack of communication about a Q-fever outbreak in goats caused more than 3000 reported human Q-fever cases. Q-fever, caused by the intracellular bacteria *Coxiella burnetti*, causes little symptoms in animals. If symptoms do occur, they can mainly be identified as abortion. Besides inhalation of bacteria and consumption of contaminated raw milk, infection can be acquired through contact with placentas or birth fluids of infected animals as the bacterial load in these tissues is enormous (Eldin et al., 2017). *C. burnetti* can cause pneumonia, liver damage and endocarditis in humans and is a feared bioterrorism agent (Eldin et al., 2017). *C. burnetti* is endemic all over the world, New Zealand as exception. Until the outbreak in the Netherlands, Q-fever was mainly associated with farmers, veterinarians and people employed in slaughterhouses. However, during the outbreak in 2007-2010 it is estimated that more than 40,000 people were infected without any previous contact with carrier animals (Eldin et al., 2017). It is assumed that due of the expansion of dairy goat farming in those areas, more carrier animals of *C. burnetti* were introduced. The presumed cause of people getting infected is due to the fact that bacteria released during abortion might have ended up in the manure and subsequently on fields from which the wind could have spread the bacteria to nearby towns and villages (Enserink, 2010). The main reason of this outbreak reaching such a large extent is attributed to a lack of provision of information from the veterinary community towards public health authorities despite it being a notifiable disease. A public health strategy was set up in spring 2008, however control measures were inefficient (Eldin et al., 2017). As economic losses for farmers are limited, there was little incentive for farmers and veterinarians to cull the animals. As a result of a lack of cooperation, often driven by external factors such as different goals and economic interests, human health was compromised (Enserink, 2010).

1.1.4.2 Shared health costs

An important aspect of OH in terms of costs is that this approach enables sharing health costs and facilitates resource allocation across sectors. Therefore, increased cost-efficiency and cost effectiveness is expected leading to organizations, and partners to be more likely to invest in a OH approach which is turn beneficial for the 3 domains of health (Baum et al., 2017). Rabies is an excellent example of where the costs and benefits of zoonotic disease control measures are not fairly distributed across sectors. It is the human health sector that derives most of the benefits from prevention and control against rabies in endemic areas, while the veterinary sector is generally responsible for control in dogs and the associated costs, e.g. via monitoring and vaccination. Without a division of costs and benefits between sectors, veterinarians might be reluctant to prioritize investments around rabies control, due to the non-existing economic value of dogs compared to the control of endemic diseases in livestock with economic importance (Cleaveland et al., 2014).

In the study ‘Benefits of a OH approach: An example using Rift Valley Fever’ researchers examined the value of a OH approach for scientific and resource benefits (Rostal et al., 2018). The study evaluated the transport costs for the epidemiological study of Rift Valley Fever in sub-Saharan Africa (SSA) for the duration of 2 years. Implementing OH and sharing the vehicle between investigators for human, animal, vegetation and soil investigators; lead up to 31% less trips needed and there was a total save of 35% in transportation costs. These results indicate that a OH approach could be cost-efficient than a traditional approach and saved money can be reallocated within the project (Rostal et al., 2018).

Another study, implementing a OH approach through the mass vaccination of livestock to improve human health related to the zoonosis brucellosis, estimated the economic benefits and cost-effectiveness of a OH approach in Mongolia (Roth et al., 2003). Brucellosis has a significant impact on human and animal health, and has also major socio-economic consequences, especially in areas where livestock represents a major source of nutrition and income. This case study showed that vaccinating livestock cost 8,3 million USD, but that the ultimate benefit, through improved animal production and fewer human health problems, amounted to 26,6 million USD which represented a benefit-cost ratio of 3.2. This strategy would be feasible and cost-effective for health sectors as well as agricultural sectors, if those sectors would bear the costs of vaccinating livestock in relation to the benefits (Roth et al., 2003). These findings support the idea that through shared efforts on disease control and detection, efficiency and cost-effectiveness increases within sectors (Baum et al., 2017).

1.1.4.3 Research

The OH approach in terms of research leads to an enhanced understanding of health impacts and solutions. By taking multiple dimensions into account, researchers may discover new insights and holistic problem solving through a more adapted intervention design (Lebov et al., 2017). The ultimate aim of OH research is to gain new opportunities for health improvement and to enhance risk mitigation for humans, animals and the environment (Lebov et al., 2017). In addition, OH highly promotes integrated ways of data sharing, especially in research. For instance, data sharing by epidemiologists, regarding the different types of circulating influenza viruses in animals, towards humane vaccine developers is essential (van Herten et al., 2019).

1.1.5 The implementation of One Health to tackle today's complex problems

Besides infectious diseases, to date the world suffers from rapid environmental changes which include the increase of the human population, from 1 billion in 1800 to 7,7 billion today[5], increasing industrialization and climate change. These changes put a continuously strain on global health which results in complex health problems such as Antimicrobial Resistance (AMR), problems involving food safety and - security and emerging infectious - and zoonotic diseases. These problems can be considered as consequences of human behavior and activities. Therefore, the only way forward is through informed decisions regarding human, animal and environmental health, taken from a multidisciplinary and integrated point of view involving all relevant sectors (Destoumieux-Garzón et al., 2018).

1.1.5.1 Emerging- and zoonotic diseases

It was the emergence of several zoonotic diseases that set the OH concept in motion. Even now emerging zoonotic diseases keep posing a threat and remain in the spotlight. During a consultation held by the FAO/WHO/OIE in Geneva in 2004, emerging zoonoses were defined as newly recognised diseases or diseases that have been known but of which the incidence, geographic location, vector or host distribution has changed or increased (WHO-FAO-OIE, 2004). Although some zoonotic diseases have been well established and have been around for much longer, it is precisely in recent decades that they have been on the rise. Factors that are partly responsible for this emergence are globalization, environmental changes (e.g. climate change), farming practices and close coexistence and overlapping habitats of humans, domesticated animals and wildlife. Especially wildlife appears to be an enormous source of the development and transmission of new zoonotic diseases (Wang and Crameri, 2014).

As illustrated in Figure 2, 60 % of infectious organisms are zoonotic and thus have the potential to affect both humans as well as animals. In addition, 75% of these emerging infectious diseases are of animal origin, 3 new human diseases of animal origin develop each year and 80 % of the agents that pose a threat through bioterrorism are zoonoses. These statistics emphasize more than ever that humanity

[5] https://ourworldindata.org/world-population-growth (last consulted March 2021)

must take action to protect itself against the potentially destructive consequences of these emerging- and zoonotic diseases as their upward trend is expected to continue.[6]

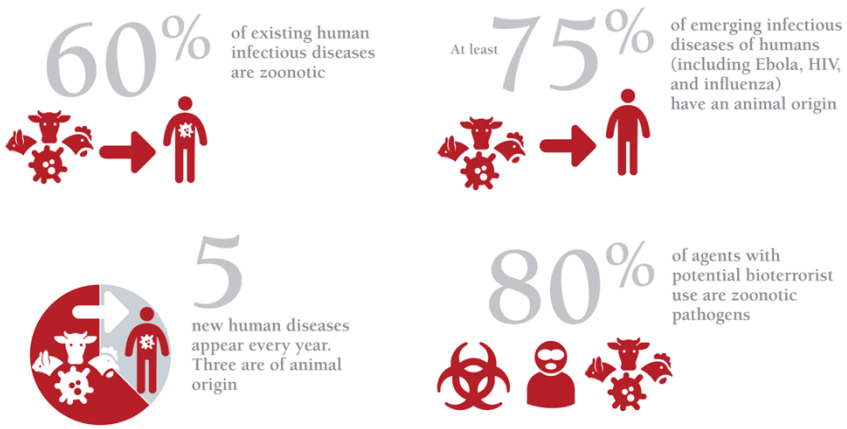

Figure 2. Estimations on zoonotic diseases (OIE, 2009)

The list of emerging zoonotic diseases is long. However, the spill-over, from bats to human populations, attracts attention as many zoonotic viruses arise from these animals. Among the *Paramyxoviridae*, Hendra and Nipah virus can be cited, viruses belonging to the *Coronaviridae* include severe acute respiratory syndrome, middle east respiratory syndrome and coronavirus disease of 2019 (COVID19). Ebola and Marburg viruses, both *Filoviruses*, are high on the list of the deadliest viruses to humankind and have caused an enormous mortality rate of Great Apes in Central Africa (Wang and Crameri, 2014). Bats are considered as the natural reservoir of these viruses, yet most human infections are acquired through the slaughter and consumption of wild animals and non-human primates (Leroy et al., 2009) .

While many viral emerging zoonoses come from bats, these animals are not the only source of various infectious zoonotic diseases. West Nile Virus is transmitted via mosquitos, which act as vectors, between birds, mammals and humans.[7] Additionally, some non-viral zoonotic diseases are re-emerging in certain regions, including rabies, brucellosis and parasitic diseases such as cysticercosis/taeniosis.[8] Other non-emerging or re-emerging zoonotic diseases that currently pose a threat include anthrax, Ebola, Lyme disease, rabies, West Nile virus infection, avian influenza, babesiosis, botulism, brucellosis, giardiasis, leptospirosis, listeriosis, trichinellosis, Creutzfeldt-Jakob disease and Q-fever.[9]

1.1.5.1.1 One Health to tackle emerging- and zoonotic diseases

Zoonotic diseases arise from the intertwined relationship between humans, animals and the environment. Consequently, it is important to take the evolutionary circumstances and pathways of disease transmission into account in order to find effective and sustainable disease management strategies. To make this possible, there is a high need for collaboration between field specific professionals (Webster et al., 2015). Therefore, the concept of OH has become the international standard for control, research and surveillance of zoonotic diseases. In order to provide guidance for countries to tackle zoonotic diseases, the WHO/FAO/OIE tripartite set up 'A Tripartite guide to addressing zoonotic diseases in countries'. This document provides the definition of OH, offers guidelines and operational tools for countries to support them in finding sustainable health solutions for endemic and emerging zoonotic diseases, zoonotic disease events and other threats involving the human-animal-environmental interface. The guidelines provide tools to facilitate problem solving i.e. models for standard operating procedures to facilitate the OH approach by governments (FAO/OIE/WHO, 2019).

[6] https://www.oie.int/en/what-we-do/global-initiatives/one-health/ (Last consulted April 2021)
[7] https://epidemio.wiv-isp.be/ID/diseases/Pages/WNV.aspx (Last consulted March 2021)
[8] https://www.who.int/zoonoses/emerging_zoonoses/en/ (Last consulted March 2021)
[9] https://www.ecdc.europa.eu/en/zoonoses (Last consulted March 2021)

Zoonotic diseases in animals are often not noticed, until they breach the species barrier and humans become infected. Following the report of human disease, emergency measures are implemented to prevent spread in human populations and to find the source of the infection in the environment or in animals. When animals can be identified as the source of disease outbreak and they pose a continuous threat to humans, it is often decided to cull these animals leading to severe economic consequences (Heymann and Dixon, 2014). Current cooperation between animal and human medicine sectors is ought to improve joint disease surveillance and risk assessment to detect outbreaks earlier and limit damage. In addition, researchers are currently investigating geographic predilection sites, or sites with a past of zoonotic disease outbreaks, by sequencing and identifying infectious organisms in tropical animals and wildlife. Hereby, predictions about future zoonotic disease outbreaks from wildlife to humans can be made (Heymann and Dixon, 2014).

Although the current paradigm in which surveillance, identification of disease outbreaks and measures taken may be effective, it is not sustainable nor cost-effective. It is especially important to learn from transient disease outbreaks and to focus on preventing the onset of zoonotic diseases at the source (Heymann and Dixon, 2014). Key in shifting the paradigm is managing infection and disease outbreaks in human populations, the prevention of transmission and predicting emergences and to control animal populations where feasible. This approach can only be successful when the influencing factors and the causal relationship with the environment and its effect on the occurrence of animal infections is completely understood. Therefore, a collaborative OH cooperation between epidemiologists, veterinarians among other field specialists is needed (Heymann and Dixon, 2014). Additionally, preventative measures must go in both ways as many zoonotic diseases can be passed in reverse causing healthy livestock to be infected (Zinsstag et al., 2018).

Many countries undertake national measures to combat the prevalence of certain zoonotic diseases. The best possible outcomes can be obtained when preventive measures stop the disease from entering the country. In South Korea for example, it has been shown that the main causes of pathogen introduction are the illegal import of wild animals, travelling beyond national borders and the migration of wildlife. Since these critical points are known, it is becomes clear which control measures can be taken to limit possible disease outbreaks (Zinsstag et al., 2018).

1.1.5.1.2 One Health as an answer to neglected zoonotic diseases

As little is often known about these rapid emerging zoonotic diseases concerning virulence, source, distribution and the lack of adequate identification and control measures, these diseases often get significant attention mainly driven by fear (Rupprecht and Burgess, 2015). Besides these emerging zoonotic diseases, there are other endemic zoonotic diseases that cause enormous health and socio-economic consequences. However, these zoonotic diseases are often forgotten since they are not ‘newly emerging’ and have been eliminated in wealthier countries. Therefore, these zoonotic diseases are referred to as ‘neglected zoonotic diseases’. Neglected zoonotic diseases include rabies, brucellosis, *Taenia solium* (neuro)cysticercosis, cystic echinococcosis, bovine tuberculosis and leishmaniasis along with 10 other diseases (Welburn et al., 2015).

Low- and middle - income countries in particular have a hard time suffering from neglected zoonotic diseases as appropriate disease control often lacks due to various factors including governmental-, political- and economic issues and the lack of knowledge (Cleaveland et al., 2017; Halliday et al., 2015). Other reasons for this neglect can be attributed to under-reporting which leads to an underestimation of their global burden. Therefore, their relevance is often underestimated which leads to less motivation by policy makers and funding agencies to act and to assess the disease burden, effectiveness of control and intervention strategies (Cutler, 2015). Due to the fact that intervention costs can seem high to donors and policy makers, it is necessary to provide them with evidence on disease burden and costs, cost-effectiveness of integrated control and elimination options, economic benefits for the livestock sector and the benefits of sharing costs across sectors (Welburn et al., 2015). This evidence may be the final push to persuade donors and policy makers to implement a OH approach to tackle these neglected

zoonotic diseases as the only sustainable solutions require cross-sectoral, integrated approaches in the long-term. In addition, every intervention must take sociological, economic, political, biological and environmental factors into account in the target population (Welburn et al., 2015).

1.1.5.1.3 Successful One Health approaches regarding zoonotic diseases

An excellent example of different sectors jointly responding to an emerging zoonotic disease is the Hendra virus outbreak. In 1994, a disease outbreak of unknown cause occurred in Queensland, Australia. Horses were affected of which 11 had died, the trainer, closely related to the horses also showed severe symptoms suggesting the same disease. The nation immediately bundled efforts in order to identify the cause and source of this disease outbreak. The research team consisted of researchers from governmental public and animal health agencies, the Commonwealth Scientific and Industrial Research Organisation and the Australian Animal Health Laboratory (Wang and Crameri, 2014). Close collaboration took place within the research team of virologists, public and animal health experts and lab workers, sharing findings and results in a rapid pace. As a result of this integrated approach, the virus, later called Hendra virus, could be isolated from a dead animal within a week after the initial start of the outbreak. On the 7th day, an antibody test was available which facilitated the measurement of infection rates in both humans as well as animals. After 2 weeks, it was confirmed that the horse trainer indeed suffered from a Hendra virus infection (Wang and Crameri, 2014). Studies were conducted on a large scale and in subsequent years, it was discovered that bats belonging to the genus *Pteropus* were the wild-life reservoir of the virus. Although, the virus is not directly transmissible from bats to humans, and no evidence of persistence circulation in horses/ humans was found a vaccine was developed rapidly to prevent the spread from infected horses to humans. Although 89 horses have died, and 7 people became infected, of which 4 died, worse could be prevented. Thanks to this swift action, and seamless collaboration of disciplines, this disease outbreak was halted in record time and its efforts received worldwide praise (Wang and Crameri, 2014).

The health burden of rabies, a zoonotic pathogen, is immense due to its notorious lethality, yet it is considered as a neglected zoonotic disease in African and Asian countries.[10] All sorts of mammals including humans can get infected by rabies. The two cycles of transmission, sylvatic and non-sylvatic, make this disease challenging (Acharya et al., 2020). Most human cases of rabies are caused by dog bites. Upon infection timely reporting and the administration of a post-exposure prophylaxis is crucial to safe the patient's life. However, in many poor areas this is not possible leading to high mortality rates (Davis et al., 2015).

Despite its lethality, rabies is considered a manageable disease, especially when comprehensive, strategic and targeted control is implemented i.e., prevention of the disease in both humans and animals. As dogs pose the greatest threat to humans getting infected, preventing rabies in dogs is a major step forward from focusing solely on prevention or curative treatment of human cases (Acharya et al., 2020). In Nepal, an action plan is set up in which the objective is to no longer have human deaths from rabies by 2030. A national guideline for rabies is applied here, whereby a mass vaccination of dogs takes place, but also of livestock. In addition, people are vaccinated (Acharya et al., 2020). The researchers state that rabies can be prevented or managed efficiently with the implementation of a OH approach involving intersectoral collaboration among animal, human and environmental health, which stresses the effectiveness of this approach (Acharya et al., 2020).

These statements can be supported by the rabies occurrence in Latin America, where the greatest successes in the last decades regarding rabies control have been achieved. As a result, human deaths are now rare, and there is a tremendous decline in the prevalence of canine rabies (Belotto et al., 2005). This achievement can be attributed to the strong political and executive commitment started by Pan American Health Organization in America during the 1980s. Their regional control program implemented mass vaccination in dogs and provided greater surveillance in the human health and veterinary sectors. The importance of mass dog vaccination has been recognised by the Department of Health, and in most

[10] https://www.cdc.gov/rabies/location/index.html (Last consulted March 2021)

Latin American countries, mass dog vaccination campaigns are conducted annually or bi-annually by health authorities. This involves large-scale deployment of veterinarians as well as education (Vigilato et al., 2013).

1.1.5.2 Antimicrobial resistance

Although antimicrobials once were considered as 'wonder drugs', the world now faces AMR threatening the ability of treating infectious diseases on a large scale (McEwen and Collignon, 2018). The paper 'Tackling drug-resistant infections globally: final report and recommendations' predicts that if no action is taken, by 2050, 10 million deaths each year will be attributable to AMR, and its cumulative cost will be around 100 trillion USD.[11] These shocking results emphasize the need for action and measures to call this situation to a halt.

The interconnection between human, animal and environmental habitats contributes to the development and spread of AMR. The massive use and abuse of antibiotics and other antimicrobials in human, animal and environmental sectors can be cited as causal links for the occurrence of AMR. In addition, most classes of antibiotics in particular used in humans are also used in animals to treat bacterial infectious diseases (Laxminarayan et al., 2013). Additionally, the contamination or introduction of antibiotic resistant strains in the environment poses a threat (Hernando-Amado et al., 2019).

Given the interdependent nature of AMR in the human-animal-environmental interface, implementing a OH approach to address this problem is a logical step forward. Uniform measures and guidelines on antibiotic use in the animal health, agricultural as well as in the human health sector were urgently needed (McEwen and Collignon, 2018).

As a response, global efforts have been made by international agencies e.g. WHO, OIE, FAO and individual countries to develop comprehensive action plans on antibiotic resistance (McEwen and Collignon, 2018). The WHO has been committed to AMR since the 1990's by organising multidisciplinary activities, establishing consultation and advisory groups, providing scientific evidence on the harmful effects of antibiotic use in humans and animals, and of AMR. In addition, the WHO suggests recommendations for all interests such as public health, veterinarians, pharmaceutical industry and the animal production industry including farmers (WHO, 2000). Subsequently, the WHO launched a global action plan in 2015, which embraces the concept of OH in the search for new strategies and solutions and states 5 objectives to address AMR. (1) improved awareness and understanding of AMR through effective communication and training, (2) to strengthen the knowledge and evidence base through surveillance and research, (3) reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures, (4) optimizing the use of antimicrobial medicines in human health and (5) to develop the economic case for sustainable investment that takes account of the needs of countries and to increase investment in new medicines, diagnostic tools, vaccines and other interventions (WHO, 2015). In addition to the existing guidelines, additional guidelines were launched by the WHO in 2017 aiming to tackle the excessive routine use of antimicrobials by farmers in food-producing animals in particular (WHO, 2017).

The European Union (EU) is also committed to invest in a OH approach regarding AMR. An EU response to this complex problem is the establishment of the 'European One Health action plan against antimicrobial resistance' to enable an integrated approach at international level. This action plan is based on the principles of OH and the overarching goal is to maintain the ability to treat infections in humans and animals. This approach is considered as an example for third countries due to the fact that it is proactive, policy-oriented, consistent and it provides international standards and information/evidence on AMR (McEwen and Collignon, 2018).

[11] https://www.biomerieuxconnection.com/wp-content/uploads/2018/04/Tackling-Drug-Resistant-Infections-Globally_-Final-Report-and-Recommendations.pdf (Last consulted March 2021)

The action plan provides a framework and scope for new, more comprehensive measures to combat the emergence of antimicrobial resistance and to increase availability and development of successful antimicrobials both inside and outside the European Union. Mentioned action points are for example creating more integrated surveillance systems. Since resistant microorganisms harbor in humans, animals and the environment, antibiotic resistance is a complex epidemiological problem. To avoid abuse of antibiotics at the human-animal-environmental interface, an extensive One Health-based surveillance system on the use of antimicrobials is needed to be able to respond to AMR and to come up with appropriate solutions in addition to current antibiotic surveillance systems. There is additionally a high need for the provision of evidence from health institutions to create awareness surrounding antibiotic resistance, improved coordination and implementation of EU rules, improved prevention and control measures, a better understanding of the role of the environment in the development of antimicrobial resistance, the stimulation of research in new therapeutics and preventive vaccines, collaboration with developing countries and the development of a global research agenda (European Commission, 2017).

As European AMR efforts to collect clinical AMR data by veterinarians in animals is still considered below par, the new framework 'European Resistance Surveillance network in Veterinary medicine' was proposed. This surveillance network aims to improve reporting on AMR, monitor trends and to detect emerging AMR pathogens in animals and livestock. To ensure a OH approach, EARS-vet aims to be complemented with other AMR monitor systems to facilitate cooperation and the sharing of results (Mader et al., 2021).

At national level, Belgium is currently developing a One Health national action plan considering AMR from human, animal and environmental perspectives.[12]

1.1.5.3 The environmental crisis

Maintaining public health on a planet threatened by polluted air, soil and water, deforestation and global warming is unmanageable. In order to find sustainable solutions to deal with the earth's changing processes and upcoming risks, intersectoral collaboration is highly needed (Zinsstag et al., 2018). At global level, OneHealth and EcoHealth, two separate organisations, undertake effort to find sustainable solutions as addressing OneHealth issues without respecting ecological health is impossible (Mi et al., 2016).

1.1.5.3.1 Global warming

Especially global warming has the potential of destructing effects on health in general. Temperature on earth has been gradually increasing since the 1950s and is primarily caused by the production and release of greenhouse gases and fossil fuel burning.[13] The effects of global warming are significant and include increasing periods of extreme drought, heat waves, floods and storms and melting of glaciers and sea ice with rising of the sea level as a direct result. These consequences in turn have an enormous negative impact on many sectors due to the spread of infectious diseases, increased mortality of heat stroke and changes in food productivity and housing due to flooding (Evans and Leighton, 2014; Smith et al., 2015; Zinsstag et al., 2018). Since global warming is a continuous process (Schellnhuber, 2008), integrated solutions must be found to address the problems that directly and indirectly arise from it, as illustrated in the following sections.

Climate change plays a significant role in the spread of vector borne diseases as certain vectors, i.e., mosquitos, thrive in the warming northern climates. As a result, certain diseases, such as malaria and yellow fever, are on the rise in the Northern Hemisphere. To be able to anticipate on the current climate change and to prevent vector borne diseases, integrated surveillance must be taken into account. When vector borne- and emerging diseases can already be detected in the vector, livestock or wildlife itself,

[12] https://www.health.belgium.be/nl/bestrijding-van-antimicrobiele-resistentie (Last consulted March 2021)
[13] https://earthobservatory.nasa.gov/features/GlobalWarming/page2.php (Last consulted March 2021)

action can be taken early in transfer, preventing illness and costs in terms of human health (Zinsstag et al., 2018).

Another example of the negative influence that climate change has on the spread of disease in the environment is Leptospirosis. Leptospirosis is a widespread zoonotic disease of great importance to human and animal health (Levett, 2001) and can be considered as a re-emerging disease (Mwachui et al., 2015). Recent studies have shown that increased precipitation and flooding due to climate change has an influence in the occurrence of leptospirosis in humans due to the fact that contact with contaminated water (via urine of infected mammals) facilitates infection (Mwachui et al., 2015).

Pollution of the environment is another problem to be addressed as it not only occurs through the discharge of chemical contaminants. It is of great importance that the processing of human and animal excrement is conducted safely. One of the effects of global warming is in fact the increased frequency of periods of high precipitation (Attema et al., 2014). High amounts of precipitation pose an increased risk of pesticides (Donald et al., 2007) and human or animal faeces being flushed from fertilized meadows and fields to drinking water sources. Uptake of contaminated water can lead to health consequences due to exposure to pesticides and the presence of faeces likely to be contaminated with zoonotic pathogens (Sterk et al., 2016).

1.1.6 Limitations of a One Health approach

While a OH approach has proven valuable in addressing AMR and in tackling emerging zoonotic diseases, the concept also receives resistance of some critics and public debate towards moral, institutional and funding dilemmas.

1.1.6.1 Moral dilemma's

Since OH stands for protecting human, animal and environmental health, many argue whether standard institutional responses on outbreaks of zoonotic diseases, resulting in mass culling animals, fits this concept as animals who are culled, are infected, might be infected or are a potential carrier (Meijboom et al., 2009). In applying OH a balance has to be found between human interests and the well-being of other non-humans (Degeling et al., 2016). The way in which European animal disease policies find their justification for culling animals is through the 'harm to other' principle. This principle can be explained broadly as the fact that individuals can act upon their own liberties and choices unless these actions can cause harm to another individual. Unfortunately conflicting claims are often made by stakeholders who expect to be harmed due to the outbreak of zoonotic diseases or in the prevention of notifiable diseases, with devastating effects on animal populations (Meijboom et al., 2009). Subsequently, animal interests are disregarded when traditional public health measures, i.e., culling of animals often part of a OH approach, form the direct answer to zoonotic diseases. Indeed, harm to animals can never be completely avoided, so it is important to look for considerations between human and non-human interests (Meijboom et al., 2009).

1.1.6.2 Conflicts of interest and implementing policy changes

OH paves the way for closer cooperation between partners, organisations and institutions towards the common health of the 3 domains. It takes a lot of effort and dedication to actually make different sectors work together harmoniously, as they often have different ideas and views, priorities and even funding. Unfortunately, it has turned out that sustainable partnerships are no longer achievable once funding ends (Stephen and Karesh, 2014). Especially the funding of animal- and environmental health has proven to be difficult compared to human health, due to the fact that most nations do not invest in institutions whose main mission is animal disease prevention, control and surveillance (Kahn, 2012). Additionally, conflicts of interest might arise in zoonotic disease control which challenges an integrated approach e.g. between public health institutions and disease control (van Herten et al., 2019). Also,

some authors have noticed that human medicine's investment in OH discussions was poor and that there is lack of the involvement of stakeholders from the environmental sector (Häsler et al., 2012).
Furthermore, implementing OH can be challenging in initiatives where infrastructure, personnel and funding have been already allocated, or where there is a shortage of resources. The OH community therefore faces the challenge that requires the creation of long-term cross-sectoral collaborations that can transcend the need and difficulties surrounding funding, and must find ways to integrate the concept into ongoing initiatives which is not always self-evident (Sinclair, 2019; Stephen and Karesh, 2014).

Before changing the policy towards the OH approach, governments and decision-makers often need proof of the positive influence that the changed policy will create. Unfortunately, this is also the case for the implementation of OH (Sinclair, 2019). Despite the fact that the OH approach has already provided perspective on AMR and tackling emerging zoonotic diseases, there is still a demanding need for measurable proof of the positive impact of a OH approach. Additionally, the shortage of practical and tested operational methods for the execution and metrics for the evaluation of One Health limits the implementation of the concept by authorities (Baum et al., 2017).
As implementing this approach requires initially new investments, procedures and systems to enable coordinated collaboration across disciplines and requires a lot of effort and money, this evidence is urgently needed. This all leads to the remaining question of what kind of information is needed to convince decision-makers and how cost savings and impact can be measured,- so that decision makers are more willing to implement this approach in their policy (Sinclair, 2019).

1.1.6.3 Sector inequality

Although the OH approach aims to involve all interested sectors and great progress has already been made in the shift towards transdisciplinarity, the OH approach is mainly veterinary oriented as the environmental and medical sector remain underrepresented (Barrett and Bouley, 2015). The reason given is that due to differences concerning political, status and income between physicians and veterinarians, physicians are reluctant to adhere to this approach which mainly consists of veterinarians. Moreover, in a OH approach, health problems are often discussed more frequent while the driving environmental factors important for these health issues are often less prominently brought to the attention (Barrett and Bouley, 2015). Joint efforts and communication between the One Health and EcoHealth organisation might help to overcome the gap of underrepresented environmentalists in the OH approach (Mi et al., 2016). The OH community faces this challenge and must find ways to be able to involve all sectors in a balanced way (Gibbs, 2014; Mi et al., 2016).

1.1.6.4 The need for expansion of the One Health approach

Social and contextual epidemiological factors play a major role in the transmission of zoonotic diseases at individual and community level. Examples of factors are gender, social norms, community dynamics, and settlement patterns. Although the OH approach enhanced the change in research and (endemic) disease prevention/ responses to outbreaks, some researchers mention that the OH approach solely focusses on the broader outlines of drivers and risk factors that influence zoonotic disease transmission between wild and domestic animals to humans in the environmental context without regarding the more complex social and contextual factors (Woldehanna and Zimicki, 2015).

Complex factors that influence disease outbreaks can be taken as an example to stress the importance of expanding the OH approach. The main drivers causing disease in wildlife and facilitating zoonotic disease outbreaks, described by the OH approach include human induced habitat changes (e.g., deforestation, mining and the construction of plantations, road construction and pollution), transport of - and trade in animals and the consequences of increased animal-human contact through more intensive production systems. It is indeed those events that influence zoonotic disease outbreaks, but it is certainly important to subsequently take human interaction at the local level into account. Especially the 'if, how, where and when' questions concerning interaction between people and animals must be further looked into (Woldehanna and Zimicki, 2015).

To stress the importance of those questions, a study concerning the first documented Nipah virus outbreak in Malaysia can be taken as an example. This study states that several different sociological and ecological factors were at the basis of an accelerated outbreak of the Nipah virus in 1999 in humans as well as pigs. Factors influencing this outbreak included drought due to El-Niño, change in land use i.e., deforestation leading to the reduction of fruit bat habitats, and the forced relocation from bats to orchards due to slash-and-burn farming practices. In addition, pig stables were located near orchards and their construction allowed the entrance of fruit remnants eaten by bats. As a result, pigs required infection via saliva-contaminated fruit, and passing the infection on to their handlers (Chua et al., 2002).

So indeed, the previous mentioned drivers are important, but it is even more important to pay attention to the more specific social and ecological determinants, which is why the paper 'An expanded One Health model: Integrating social science and OH to inform study of the human-animal interface' proposes an expanded OH model that takes all those sociological and ecological determinants int account that contribute to disease emergence at local level (Woldehanna and Zimicki, 2015)

1.1.7 The need for evaluating the One Health approach

Implementing OH in an initiative is a vast step forward, but evaluation of the currently implemented OH projects, systems and initiatives is necessary. An evaluation provides feedback on how well these initiatives function, what they contribute to, the potential problems they may encounter and how much OH they really are. Quantitative measurement of cost savings or effectiveness within OH programs additionally provide valuable evidence of efficacy. These results lead to insight into the added value of a multidisciplinary collaboration and contributes to obtaining future funding. As described in section 1.1.6 'limitations of a One Health approach', the lack of evidence of the benefits of an integrated OH approach contributes to a reticent attitude on the part of policymakers. Thanks to the provision of measurable data, policymakers, stakeholders, governments and researchers can be convinced more quickly to adjust their approach or policy. Although this evaluation is much needed it is yet mostly a neglected aspect in previous studies (Baum et al., 2017).

1.1.7.1 The Network for Evaluation of One Health

The Network for Evaluating One Health (NEOH) brings people with an interest in OH from a wide range of disciplines and different sectors together through an open network. NEOH's aim is to enable quantitative assessments of OH initiatives through a standardized and scientifically based evaluation protocol. To this end, the NEOH has taken various actions e.g., in addition to developing the standardized framework for the evaluation of OH, the NEOH also provides several examples of evaluations carried out in OH initiatives, provides a community of different experts of OH working together and assessing the value of OH and lastly, educates novice researchers to carry out OH evaluations.[14]

As a response to the gap of non-existing standardized evaluation frameworks to evaluate OH, the NEOH designed an evidence-based framework that allows researchers to evaluate the OH-ness of any initiative (Rüegg et al., 2018b).

The evaluation proposed by the NEOH uses mixed methods by applying both a descriptive and qualitative assessment in addition to quantitatively scoring the OH-ness of the evaluated initiative. Furthermore, the NEOH provides guidance on how to draw up recommendations based on the results obtained. This approach allows researchers, policy makers and evaluators to conduct assessments based on integrated approaches to health more efficiently (Rüegg et al., 2018b).

The evaluation tool developed by the NEOH will be explained in detail in the materials and methods section.

[14] http://neoh.onehealthglobal.net/organisation-and-partners/ (Last consulted March 2021)

1.2 *Taenia solium*

1.2.1 Introduction

T. solium is a zoonotic parasite, the pork tapeworm, responsible for a significant cross-sectoral health and economic burden due to the disease and related costs caused by human neurocysticercosis and porcine cysticercosis (Dixon et al., 2020). However, when taking the biology, transmission routes and reservoirs and the feasibility of intervening into account, human taeniosis and cysticercosis should theoretically be eradicable worldwide. While much progress has recently been made in finding new ways of control, prevention and diagnosis, it is unlikely that the parasite will be eradicated in the near future as intervention in developing countries and rural areas has particularly proven difficult (Pawlowski et al., 2005).

1.2.2 Life cycle

As illustrated in Figure 3, *T. solium* has a complex two-host life cycle involving both humans and pigs. Humans act as the final host, whereas pigs as well as humans can act as (accidental) intermediate host. The life cycle of *T. solium* starts with eggs or gravid proglottids passed on from human tapeworm carriers into the environment. These eggs remain viable for a long time in soil, vegetation, and water and are immediately infectious for pigs, whom upon ingestion develop porcine cysticercosis. Porcine cysticercosis is characterized by development of cysticerci in the muscle tissue of pigs. Infection with the *T. solium* tapeworm occurs when raw or undercooked infected pork has been consumed by the human final host. Upon infection, the tapeworm develops and lodges in the small intestine, causing taeniosis. There is usually one hermaphrodite parasite present which consists of hundreds of proglottids and with each gravid proglottid containing up to 60,000 eggs (Garcia and Del Brutto, 2000). When detached, gravid proglottids pass onto the environment with human faeces which completes the life cycle. However, as well as being infective for pigs *T. solium* eggs can also infect humans when ingested. In this stage, humans do not act as a final host but as an accidental intermediate host. This causes a tissue infection with the metacestode larval parasite leading to human cysticercosis (Allan et al., 2005). As 5 to 40% of human tapeworm carriers develop cysticercosis, self-infection and cross infection between close contacts via the fecal-oral route have been described as the main cause of acquiring cysticercosis (Del Brutto and Sotelo, 1989).

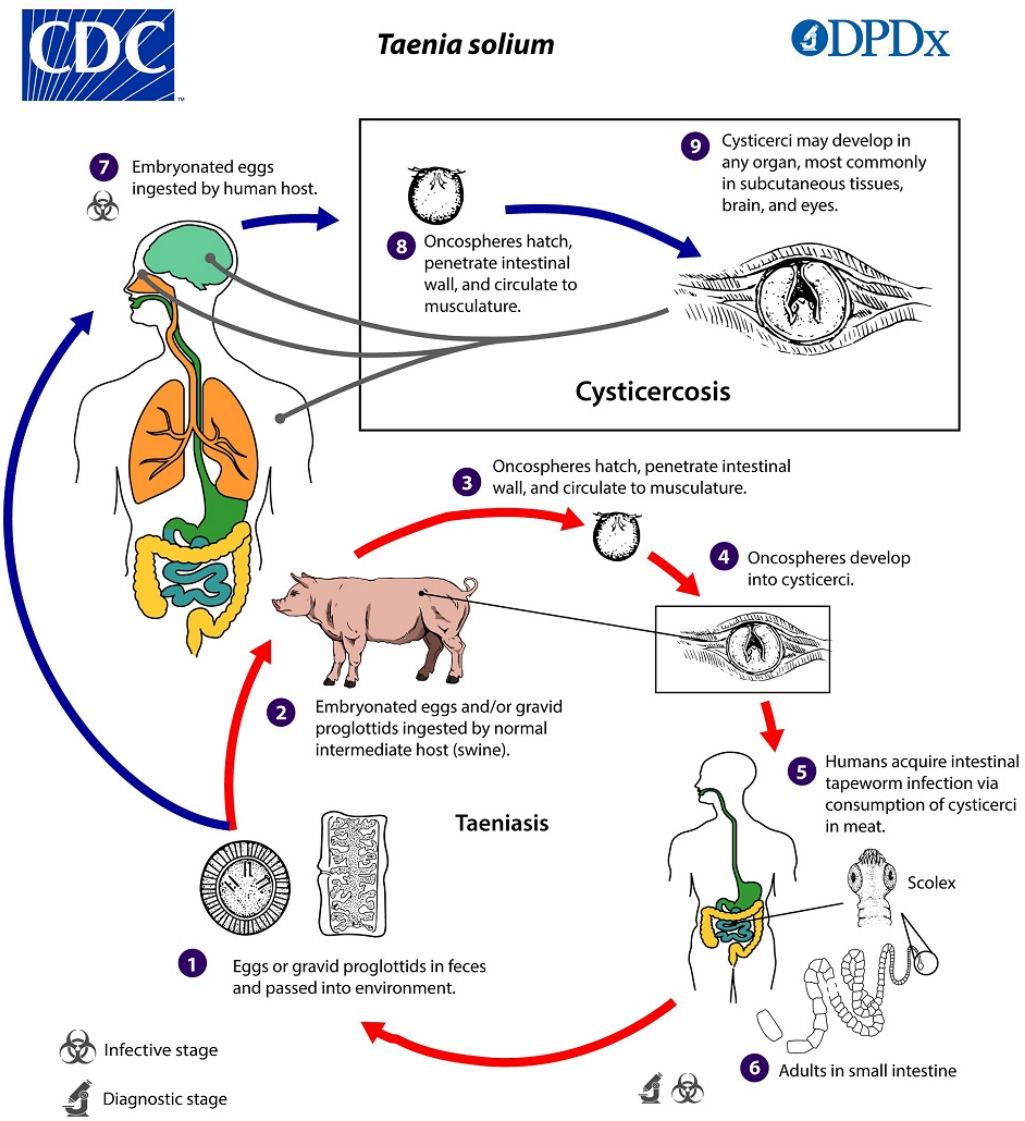

Figure 3. Life cycle of T. solium (CDC, 2019)

1.2.3 Clinical manifestations of taeniosis, neurocysticercosis and porcine cysticercosis

Taeniosis causes few clinical symptoms but if they occur, they might include abdominal pain, diarrhea or constipation, nausea, and release of proglottids (Haby et al., 2020; Mendlovic et al., 2021). However, human cysticercosis may result in much more devastating effects on human health. The larvae develop to cysticerci in the muscles, skin, eye and the central nervous system. These tissues are believed to be primarily affected due to the high blood supply (Meena et al., 2016).

In human, neurocysticercosis occurs when cysticerci develop in the central nervous system. Viable cysticerci can remain in the host for a long time, usually years, without inducing a surrounding inflammatory response. However, when cysticerci degenerate, strong immune-mediated inflammation is elicited which may result in symptomatic disease (Del Brutto and Sotelo, 1989). The number, size, location and the intensity of inflammation as a result of the host immune response can affect the severity of symptoms and clinical manifestations can range from asymptomatic to severe illness and death. Neurocysticercosis has been recognised as the most frequent preventable cause of late-onset epilepsy worldwide (Allan et al., 2005). When other symptoms occur, they might include severe headache, meningitis, convulsion and intracranial hypertension (Del Brutto and Sotelo, 1989; Garcia and Brutto, 2005).

The occurring epileptic seizures may be life threatening and eventually neurocysticercosis can be fatal due to intracranial hypertension and other complications (DeGiorgio et al., 2002).

Cysticercosis in pigs presents itself mainly as asymptomatic. Although a recent study has provided evidence that pigs suffering from neurocysticercosis can show neurological symptoms and even severe epileptic seizures (Trevisan et al., 2016).

1.2.4 The diagnosis of taeniosis, neurocysticercosis and porcine cysticercosis

Since the tapeworm carrier is most at risk of acquiring neurocysticercosis due to self-infection, diagnosis of taeniosis is crucial. The diagnosis of tapeworm carriers can be based on the presence of eggs, proglottids or the scolex (the attachment mechanism of the tapeworm to the host's intestinal wall) in stool samples. However, these are not always present, and experience is needed to distinguish the presence of proglottids/scolex of *T. solium* from other *Taenia* species, e.g. *Taenia saginata and Taenia saginata asiatica* (Flisser et al., 2004). Other methods to identify tapeworm carriers include copro antigen enzyme linked immunosorbent assay (ELISA) and the use of DNA amplification methods, e.g. specific polymerase chain reaction methods, in stool samples. However, these methods are not commercially available and their implementation in endemic rural areas would be difficult (Mendlovic et al., 2021). Another option to identify tapeworm carriers is serum enzyme-linked immunoelectrotransfer blot (EITB), which allows to detect species-specific antibodies (Allan et al., 2003).

Diagnosing neurocysticercosis is considered challenging due to the fact that clinical manifestations often are non-specific, neuro-imaging or surgical intervention is thus required although neurocysticercosis lesions are often non-pathognomonic (Del Brutto, 2012a). Magnetic resonance imaging and computer tomography are considered as the gold standard since these methods allow to assess the number, location and degenerative stage of the cysticerci. However, the use of these diagnostic methods in endemic rural areas and developing countries is not feasible because they are simply not available and there is a shortage of skilled staff in these regions (Mendlovic et al., 2021).

Tongue palpation is often used to identify porcine cysticercosis before slaughter. With this technique the tongue is inspected for the presence of cyst-like noduli which are highly indicative for cysticercosis. Yet, this technique is merely useful for heavily infected animals. In addition, porcine cysticercosis can be identified by post-mortem meat inspection. Hereby, the predilection sites i.e., the tongue, masseter muscle and heart are sliced to evaluate the presence of cysticerci. This technique has similarly to tongue palpation a rather low sensitivity (Dorny et al., 2004). Full carcass dissection has proven to be the most sensitive diagnostic tool, especially when lungs, kidney, liver and spleen are additionally examined (Chembensofu et al., 2017). The diagnosis of porcine cysticercosis can also be obtained via ELISA or EITB, however these methods are often not available (Mendlovic et al., 2021).

1.2.5 Global distribution and prevalence

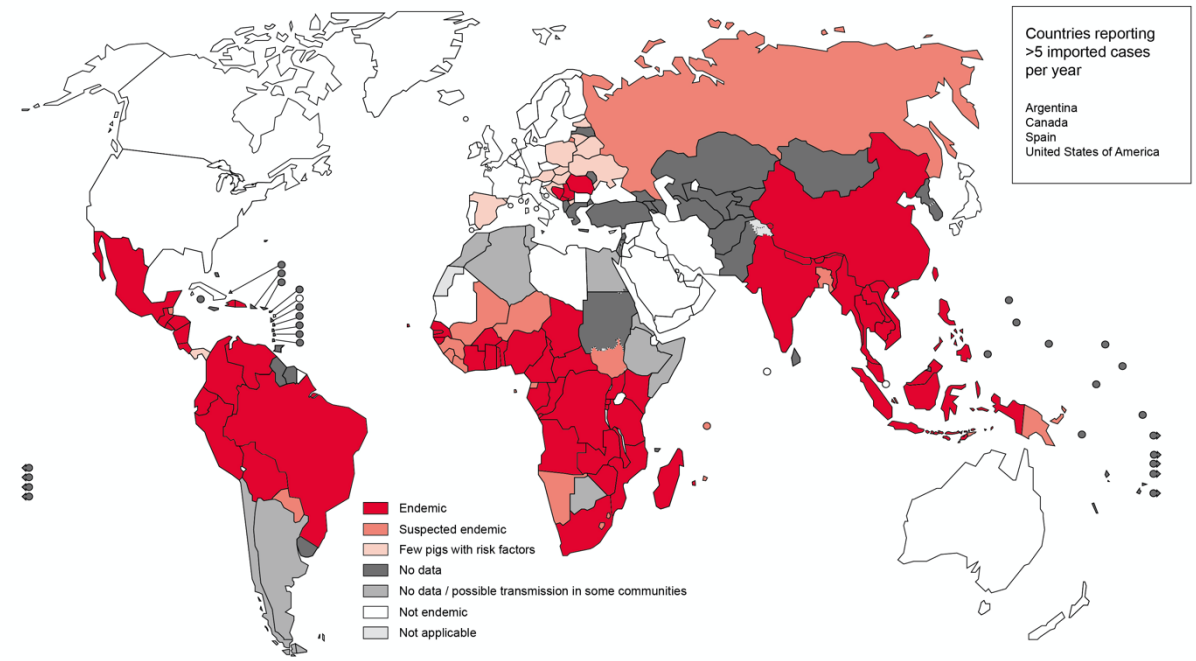

Figure 4. Endemicity map of T. solium (WHO, 2016)

As illustrated in Figure 4, the disease is mostly common in developing countries and is endemic in countries of Africa, Asia and Latin America (Allan et al., 2005). Endemicity is related to poor socioeconomic conditions, lack of public awareness about the nature of the disease, on how transmission occurs and the potential harm that it can cause to humans and poor hygiene. Especially those areas where animal husbandry and poor sanitation practices allow for pigs to come in contact with human faeces are at high risk. Due to the Koran prohibiting pork consumption, *T. solium* taeniosis and cysticercosis is rare among Muslim regions (Garcia and Del Brutto, 2000). *T. solium* has been endemic in industrialized countries such as Germany and some other countries in Central Europe in the beginning of the twentieth century. However, breaking the parasite's lifecycle and eradication was feasible due to improvement of public sanitation, increasing inspection of pork meat and especially economic development (Garcia and Del Brutto, 2000).
Nevertheless, between 1985 and 2011, 751 patients were diagnosed with neurocysticercosis in various countries of Western Europe, raising concerns of disease recurrence. Factors that can explain this trend are travel to endemic areas, increased work-related immigration in Western countries and increased pork consumption (Del Brutto, 2012b)

1.2.6 Disease burden

T. solium was ranked by the foodborne Disease Burden Epidemiology Reference Group as the most important foodborne parasite in the world, resulting in 2,8 million disability-adjusted life years (DALYs).[15] Apart from the effects on human health, *T. solium* is also responsible for significant economic costs. The major direct economic costs can be attributed to diagnosing neurocysticercosis, hospitalization and treatment. Indirect costs include productivity losses and transportation costs to the hospital (Bhattarai et al., 2015). In addition, *T. solium* has economic consequences for pig farmers as the metacestode larval stage developing in muscle, subcutaneous, and other tissues of pigs leads to reduced value of infected pork (Gabriël et al., 2017).

Providing an estimate on the economic impacts is difficult due to lack of good quality data. A cost estimation study in Mozambique showed that the economic losses for the agricultural and health sector

[15] https://www.who.int/taeniasis/epidemiology/en/ (Last consulted March 2021)

in the Angónia district, Mozambique led up to 90,000 USD annually (Trevisan et al., 2018). This cost estimation study noted that the parasite affects the livelihood of local farmers and their society by significantly reducing their societal and economic wellbeing (Trevisan et al., 2018).

Neurocysticercosis has also a high impact on society and mental wellbeing. Especially in different cultures and developing countries, people with epileptic seizures suffer from social stigma as epilepsy is often attributed to supernatural events and is considered as contagious. A study carried out in Tanzania examining attitudes towards epilepsy has found that 54,6% of the respondents attribute epilepsy to spiritual causes, nearly 30% think chances of marriage decrease, and 16,7% believe that women with epilepsy should not have children (Winkler et al., 2010).

1.2.7 Control and prevention measures

A number of control strategies have been described. Those control strategies aim at breaking the transmission cycle of *T. solium* at some point. Due to the fact that the life cycle is easy to break, previous studies have stated that *T. solium* is a potential eradicable disease (Schantz, et al, 1993). However, most of the available control strategies have only been evaluated in some small scale, scattered studies, showing varying results (Gabriel et al., 2016). In addition, some factors limit the practical implementation of control measures e.g. lack of sanitation, limited health education amongst endemic populations, poor health service infrastructure and poor socioeconomic development in certain areas (Pawlowski et al., 2005).

Control measures can be categorized into strategies tackling the tapeworm infection in the final human host or to prevent the occurrence of cysticercosis in the intermediate pig or human host.

1.2.7.1 Human-based intervention measures

1.2.7.1.1 Treatment of tapeworm carriers

Carriers of *T. solium* can be eliminated using cestodicides. Chemotherapeutic treatment of carriers can thus prevent the further spread of cysticercosis in both humans and pigs (Sarti et al., 2000). The chemotherapeutic treatment can be implemented as a mass drug administration, where every person within the population receives the treatment or it can be used as a diagnosed based treatment. The drugs, praziquantel (10mg/kg, single dose), niclosamide (2g, single dose) and albendazole (400mg/day, 3 consecutive days) are examples of registered drugs frequently used for the treatment of taeniosis (Allan et al., 1997).

1.2.7.1.2 Improved hygiene/ sanitation

Open air defecation and poor latrine maintenance are the main source of environmental contamination with *T. solium* eggs (Kungu et al., 2015). As it is assumed that *T. solium* eggs can survive in the environment for up to a year in humid conditions, food and water supply are at high risk of contamination (Jansen et al., 2021). To reduce infection risk, both in pigs and humans, improved hygiene and the use of latrines is necessary. In addition, good hygiene practices e.g., handwashing and food hygiene can prevent humans from serving as the accidental final host and can thus prevent neurocysticercosis.

1.2.7.1.3 Health education

To reach a sustained control or elimination status, education is inevitable. Human infection could potentially be prevented by changing eating habits. As cooking or boiling meat destroys the cysticerci in infected pork, these practices can prevent taeniosis. Washing vegetables that are potentially contaminated with human faeces can prevent humans from being the intermediate host and thus get neurocysticercosis. Promoting self-diagnosis of infection and improving sanitation and pig husbandry

systems are in addition important measures. However, increased awareness does not always lead to behavioral changes required to reduce disease occurrence (Gabriel et al., 2016; Gabriël et al., 2017).

1.2.7.2 Pig-based intervention measures

1.2.7.2.1 Improving pig housing and management

In developing countries, pigs often roam freely which benefits the owner by not having to invest in their feed and housing. However, the risk of ingesting *T. solium* eggs and subsequent development of cysticercosis is high due pig's coprophagic behavior and nature to root into the soil and being non-selective when it comes to food uptake. Therefore, improved pig management practices aid to reduce the access of pigs to human faeces or soil contaminated with human faeces. Interventions might be keeping and raising pigs in confinement. In addition, offering food contaminated with human faeces must be avoided (García et al., 2007).

1.2.7.2.2 Chemotherapeutic treatment of porcine cysticercosis

Anthelmintic treatment can be considered as a potential control tool. The anthelmintic benzimidazole drug oxfendazole is safe, inexpensive and has been proven to be very effective against muscle cysts as well as other endoparasites (Gonzalez et al., 2019). However, a drawback is the fact that it can take up to 6 months for the cysts present in muscle tissue to resolve, and meat to become suitable for safe consumption (Gabriel et al., 2016). With this control tool, humans can be prevented from eating contaminated meat and thus acquiring taeniosis. The withdrawal period after administering oxfendazole to pigs before being suitable for human consumption is estimated at 17 days (Moreno et al., 2012).

1.2.7.2.3 Pig vaccination strategies

A few vaccines have been successful in experimental trials and field studies. An example is a vaccine derived from larval oncosphere antigens. The vaccine TSOL18 has proven to be highly effective in the reduction of *T. solium* infections in pigs (Gauci et al., 2013). These immunizations offer a systemical immunity leading to prevention of infection. A disadvantage of immunization is the repeated vaccinations required leading to a sufficient immune response which makes vaccination a labor-intensive control or elimination measure.

1.2.7.2.4 Meat inspection

Figure 5. Presence of cysticerci in Pork (S. Gabriël)

Another control measure is the inspection of pork for the presence of cysticerci as described in section 1.2.4 'The diagnosis of taeniosis, neurocysticercosis and porcine cysticercosis'. As demonstrated in Figure 5, cysticerci in a heavy infected animal could easily be recognised. However, meat inspection is considered as a rather more ineffective measure due to its low sensitivity-level, especially considering lightly infected animals (Gabriel et al., 2016). While meat inspection can help to identify infected animals, animals in rural areas are often slaughtered in poor circumstances where meat inspection is not implemented due to this backyard slaughtering and the lack of meat inspectors (Joshi et al., 2003).

Local farmers and traders often use the tongue palpation technique. However, for obvious reasons economic loss cannot be afforded in low-income countries, leading to animals diagnosed as infected to often be sold for lower prices or slaughtered for own consumption, causing humans to get infected. Therefore, it is important to encourage villagers to adopt more hygienic slaughtering practices in rural areas and improve the standards of slaughtering facilities and free-range pig management (García et al., 2007).

1.2.8 The use of a One Health strategy to tackle *Taenia solium*

There have been prior attempts to implement control programs in sub-Saharan African conditions, however, most have been focusing on individual control options. Those stand-alone options have the potential to reduce the occurrence of the parasite, nevertheless reaching an elimination status or sustained control requires either long term or more integrated efforts (Gabriël et al., 2019, 2017). A collaborative approach, relying on the principles of OH, addresses *T. solium* control from the perspectives of human health, animal health, and the environment and is therefore essential to tackle this zoonotic neglected tropical disease.

2. Problem statement

The Eastern Province of Zambia houses almost half of the total number of pigs in the country (Mwape et al., 2015). Most of these pigs are held under small-scale management systems. The risk of pigs and eventually humans acquiring infection is heightened due to the lack of sanitation, latrines and other sanitary facilities which makes it possible for pigs to come in contact with human feces. Poor detection during slaughtering and meat processing attribute to the risk of consumption of contaminated meat. A previous study determined a high percentage of active cysticercosis infections (12,5%) in humans in the Katete district. Earlier conducted seroprevalence studies indicated that the infection rates in this area in particular are among the highest in the world and that over 50% of the acquired epilepsy cases could be attributed to neurocysticercosis (Mwape et al.,2012; Mwape et al., 2013; Mwape et al.,2015).

These results emphasize the importance of finding sustainable solutions to control or eliminate the disease in Zambia and other sub-Saharan countries which have often a similar rate of infection (Mwape et al., 2015). Intervention in this area is therefore highly needed due to *T. solium* causing enormous health and economic consequences for the local pig farmers and for the society overall.

CYSTISTOP is a seven-year intervention study evaluating the effectiveness, cost-effectiveness and local acceptability of elimination and control options of *T. solium* in Katete, a highly endemic region in the Eastern province of Zambia and was set up in 2014 lasting until 2021. This intervention study is the first large-scale integrated control/elimination program set up in sub-Saharan African conditions. The strength of the CYSTISTOP project in comparison with other *T. solium* intervention studies is the fact that this project tackles control via an integrated approach, and additionally conducts a cost estimating study which takes the local acceptability and costs required to halt the endemic situation into account. This approach is new in *T. solium* research in SSA and therefore extremely valuable (Gabriel et al., 2016). The project consists of five work packages and 3 study arms namely: an elimination study arm, a control intervention study arm and a negative study arm. The basis of CYSTISTOP consists of a multidisciplinary approach that includes both human as well as animal interventions (Gabriel et al., 2016).

Yet, while CYSTISTOP was set up with the OH approach in mind, targeting different sectors, the project designers did not intend to place great emphasis on the many facets of an OH approach. Therefore, an evaluation on the implementation of OH within the CYSTISTOP project will provide valuable information. Assessing the OH-ness allows to reflect and learn about the design of the initiative and the feasibility of its aims, i.e. implementation of integrated *T. solium* control measures, which is beneficial for future projects. In addition, quantitative measurement of the OH-ness enables comparing CYSTISTOP to other projects.

3. Objectives

The research question is the following: is the CYSTISTOP project designed and implemented according to OH characteristics and requirements?

The aim of this thesis was to evaluate CYSTISTOP on its implementation of OH using the evaluation framework developed by NEOH.
Specific objectives included:
- The formulation of assessment tools based on the NEOH framework
- The collection of data using the assessment tools
- The analysis of data according to the NEOH framework which resulted in obtaining the One Health Index (OHI) and One Health Ratio (OHR)
- The formulation of recommendations based on the outcomes of this study

4. Materials and methods

4.1.1 The Network for Evaluation of One Health evaluation tool

Few quantitative studies on the evaluation of OH have already been conducted, however these did not follow the same methodology and/or were subjectively assessed, which made interpretation of the results difficult and the results not mutually comparable (Baum et al., 2017). This stressed the need for a standardized framework to make measuring metrics regarding OH evaluation in different disciplines more accessible.

The NEOH framework describes the relationship between the operational and structural infrastructure and the changes and outcomes achieved by the initiative. This is a very important step to identify and demonstrate the added value of the integration between different disciplines and sectors, which is also the goal of an OH approach (Rüegg et al., 2018b). As a result, the comparison between OH initiatives is facilitated, which leads to increased knowledge. In addition, the obtained self-insight enables decision-making, collaboration and resource allocation (Rüegg et al., 2018b).

The evaluation proposed by the NEOH consists of 4 elements. (1) The definition of the OH initiative and its context; (2) the description of its Theory of Change (TOC) with an assessment of expected and unexpected outcomes; (3) the process evaluation of operational and supporting infrastructures; and (4) an assessment of the association(s) between the process evaluation and the outcomes produced (Rüegg et al., 2018a).

The first element focusses on the definition of the initiative and its context i.e., what the initiative stands for, and where/how the initiative is carried out. According to the NEOH approach, a OH initiative can be referred to as a subsystem that operates withing a certain context, with the aim to improve the health of humans, animals and the environment within this context (Rüegg et al., 2018b).

Subsequently, **the second element** refers to the description of the TOC. The TOC clarifies the long-term goals of the initiative, how the initiative is structured and how the initiative deals with unforeseen changes necessary to achieve its goals. In addition, the ways in which the initiative aims to achieve its objectives are described in relation to the impact of the initiative (Rüegg et al., 2018b).

Elements 1 and 2 are important preceding elements that allow the evaluator to understand what the initiative stands for. This information is essential and needs to be obtained before assessing the OH-ness of the initiative in element 3 (Rüegg et al., 2018a)

The third element evaluates the quantitative OH-ness of the initiative. To make the evaluation of an initiative's OH-ness more accessible and to quantitatively measure the added value of OH, the NEOH designed a ready-to-use Microsoft Excel spread sheet questionnaire. This tool provides the foundation needed to measure and monitor the integration of disciplines, sectors and stakeholders within a OH context (Rüegg et al., 2017).

Lastly, in **the fourth element** the OH-ness is compared with the achieved outcomes of the initiative i.e., in what extent did the integrated and interdisciplinary approach contribute to these outcomes. With the use of the TOC the processes as well as outcomes can be evaluated simultaneously. This makes determining the added value of the OH approach for the initiative feasible. Ultimately, the evaluation results in recommendations and constructive feedback from OH specialists to the concerned stakeholders of the initiative (Rüegg et al., 2018a).

4.1.1.1.1 Different aspects of element 3: the evaluation of the One Healthness

As illustrated in Figure 6, economic, social and environmental drivers of the initiative require OH operations and supporting infrastructure in order to produce the desired outcomes. These produced

outcomes ideally lead to sustainability, health/welfare, interspecies equity, effectiveness and efficiency. The term 'OH operations' entails the thinking, planning and working aspect of the initiative. The term 'supporting infrastructure' entails systemic organisation, learning infrastructure and sharing (Rüegg et al., 2017).

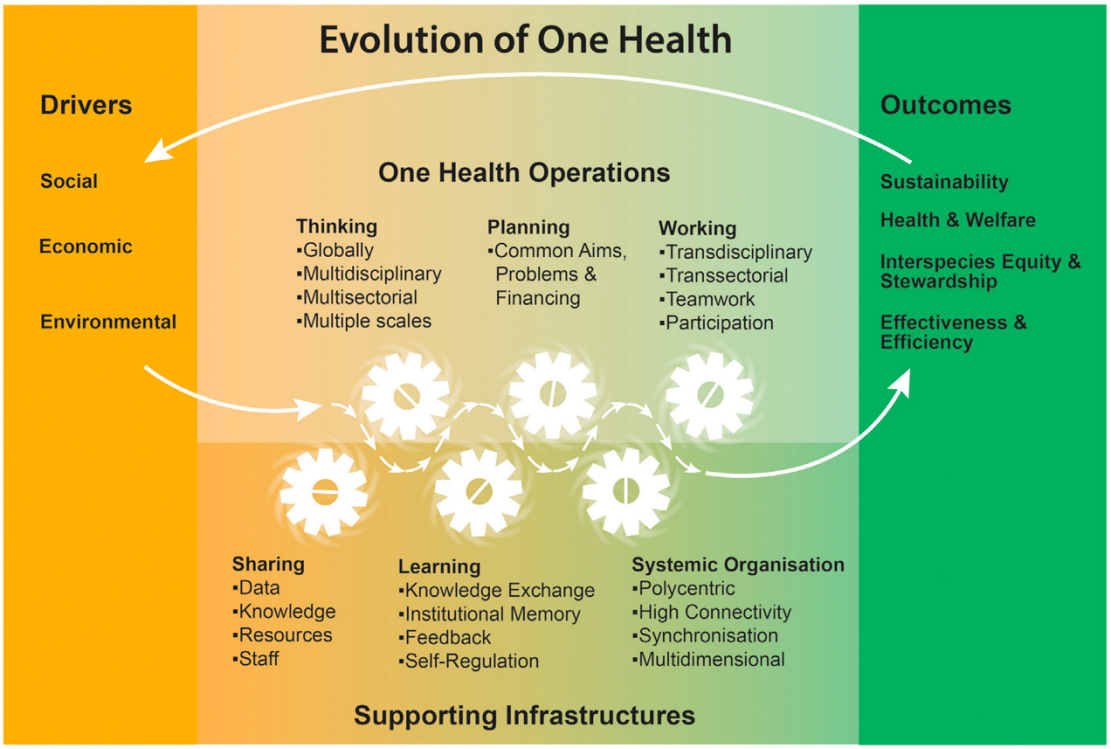

Figure 6. Visualization of the important One Health characteristics (From: Rüegg et al., 2017)

These 6 aspects are key to measure the OH-ness of an initiative, and with the use of the proposed Microsoft Excel spread sheet questionnaire, they can be scored quantitatively as scoring guidance is provided. Each aspect has its own assessment tool, based on questions that represent important criteria for a OH approach. These assessment tools are standardized for the use in different contexts. However, the questionnaire can be slightly modified, to make the questions more relevant for the initiative to be evaluated. The OH operations are evaluated through the One Health thinking, - planning and - working tool. The OH sharing, - learning and - systemic organisation tool provides questions and criteria to evaluate the supporting infrastructures of the initiative. Questions are scored with values between 0 and 1. Subsequently the median scores for each assessment tool are calculated and plotted on the spokes of a spider diagram to provide visualization about the degree of realization within each assessment tool (Rüegg et al., 2018b).

All the obtained median scores per assessment tool are subsequently summarized into a OHI and OHR. The degree of overall integration of OH in the initiative is represented by the OHI. Whereas the balance between infrastructural and operational aspects is represented by the OHR. Additionally, a spider-web diagram offers visualization of the OHI and OHR (Rüegg et al., 2018b).

The following paragraphs will clarify important criteria for OH initiatives for each assessment tool:

a) One Health thinking

The aspect of 'OH thinking' is indispensable in tackling complex problems due to the fact that thinking precedes the execution of any initiative (Whitehead et al., 2015). An all-encompassing OH approach ideally addresses multiple scales and dimensions within different factors including life, geographical space and time. Furthermore, it is important that an OH initiative fits into the context in which it will

operate and that it identifies interaction between essential systems and subsystems of the context of the initiative in order to achieve the expected outcomes. Subsequently, the initiative is assessed on how exactly it wishes to achieve change, e.g. by implementing structural change, the identification of causal connections and breaking a certain chain of events are highly representative for a OH approach (Rüegg et al., 2018a). Lastly, the initiative is assessed on how well it considers the 3 pillars of sustainability and to what degree perspectives of stakeholders and other important factors e.g. norms, values and cultural grounding impact the backbone of the initiative (Rüegg et al., 2018a).

b) One Health planning

OH planning is a direct result of OH thinking, and must facilitate ultimately decision making about priorities and objectives, to allocate responsibilities/resources and to distribute workload in order to achieve the stated aims and objectives (Yukl, 2012). Due to its complex and transdisciplinary nature, OH planning may face difficulties to keep track of what tasks, resources and actions are required in all involved disciplines and sectors making proper follow-up essential (Rüegg et al., 2018a).

Since all essential actors and stakeholders have to work flawlessly together and full engagement is required to reach a common goal, cross-sectorial and integrated planning methods are highly needed (Rüegg et al., 2018a). Furthermore, it is important to assess whether the listing of goals and responsibilities and the allocation of funding occurred independently of sectors, disciplines or organisational hierarchies through shared planning (Ledford, 2015).

The planning evaluation assesses whether several aspects such as the planned structure, location and timing, support the OH outcomes aimed for and whether the right people were heard and the right people were involved. The flexibility and adaptability as a response to non-expected outcomes are also considered in the OH planning evaluation as the ability to self-asses, learn and adapt is inherent to a OH approach. Highly flexible and adaptive initiatives will receive a high score for OH planning (Rüegg et al., 2018b).

c) One Health working

The complexity of OH problems desires people from different fields, contributing to the initiative with different skills and expertise leading to the involvement of several disciplines (Ledford, 2015). The OH approach expects initiatives to include an interdisciplinary approach which facilitates sharing knowledge and resources between different sectors, disciplines and communities (both scientific and non-scientific). In doing so, all essential stakeholders are expected to be actively involved in the process starting from defining the problem to generating and implementing solutions (Rüegg et al., 2018a). However, interdisciplinarity is not always easy to achieve, it requires commitment and intersectoral relationships (Ledford, 2015).

Essential factors that contribute to interdisciplinary collaboration can be identified as shared planning and decision-making, willing participation, shared contribution of knowledge and expertise, and a non-hierarchical structure (Nancarrow et al., 2013). However, interdisciplinary collaboration can cause friction for various reasons as interprofessional team members typically come from different sectors with different views and opinions. In addition, professionals might be more inclined to make decisions themselves within their sector, with the result that it no longer becomes shared decision making but ‘appropriate decision making’ (Gibbon, 1999). Another factor is enhancing social equality and respect regarding disciplines (and personal bound factors), as people might have prejudices about certain disciplines (Ledford, 2015).

Additionally, good leadership and management are necessary to achieve interdisciplinary cooperation and to enable joint decision making. A leader facilitates the complex communication and coordination required between the different groups of field professionals and non-professionals, has a clear direction, shared power and listens/acts upon events (Nancarrow et al., 2013).

This tool assesses how well certain disciplines work together, how well interaction between disciplines and professionals/ non-professionals is promoted, and whether there are imbalances within the initiative based on personal bound or sector bound factors (Rüegg et al., 2018b).

d) One Health Sharing

Sharing data, information and results is essential to generate knowledge. When data is shared transparently and made available to all, more comprehensive ways can be found to address complex problems. In addition, shared data can be critically evaluated from outsiders and the wider community which in turn contributes to new insights and the enhances knowledge (Rüegg et al., 2018b).

Although data sharing has many advantages, potential problems may arise that limit the efficient use of data e.g. confidentiality issues or mistrust between established collaborations, lack of transparency about what the data is used for and lack of knowledge about the benefits and risks of data sharing (Faverjon et al., 2019). Especially, sharing data on public health represents a conflict about motivational, political, legal and ethical considerations (Van Panhuis et al., 2014). However, these arguments should not outweigh the potential benefits of data sharing if done with caution and accordingly to ethical and legal principles. An interdisciplinary OH approach might help to overcome these barriers, as multiple disciplines work together in a transparent manner (Faverjon et al., 2019).

As there is a high demand for data sharing and transparency in a OH initiative, it is important to assess the ways in which data and results are shared and stored and who has access to this data. The more transparently an initiative shares his data/results, the higher the score obtained (Rüegg et al., 2018b).

e) One Health Learning

Better understanding and knowledge and processing information might lead to a change in cognition or behavior which can be referred to as ‘learning’ (Tsang, 1997). Learning occurs during every OH initiative as consequences are drawn from past events and corresponding actions are made in future decision making. Learning in OH initiatives takes individual- and group learning, as well as learning at organisational levels into account. As these 3 levels of learning influence each other, they cannot be clearly distinguished from one another (Giesecke and Mcneil, 2004).

Nonetheless, each level can be evaluated for its specific characteristics. Roughly two ways of learning are distinguished in this evaluation tool. The first is single loop learning. Single loop learning can be defined as people, organisations or groups modifying their actions according to the difference between expected and reached outcomes or errors. Subsequently, people adjust their actions to fit the issue, without reflecting the system used that led to these outcomes or errors (Jaaron and Backhouse, 2017). Double-loop learning occurs when procedures and systems are challenged as a response to errors. Double loop-learning is considered mostly valuable for organisations due to the fact that it ensures comprehensive problem solving and innovation instead of adaptation and is therefore essential in a OH approach (Maden, 2012).

An Interdisciplinary approach contributes to sharing knowledge, expertise and skills within teams/groups of people which enhances learning at the organisational level (Rüegg et al., 2018a). As learning is an important factor in a OH initiative, the assessment of ‘OH learning’ evaluates to what extent autonomous learning is promoted, the extent to what knowledge is shared within the initiative and to what extent gained information is shared and stored which all leads to changes or adjustments within the initiative (Rüegg et al., 2018b).

f) One Health Systemic organisation

As leaders are ought to facilitate individual and collaborative efforts to achieve their goal, appropriate leadership in an initiative is indispensable. Good leaders enhance team performance and have

empowering and supporting characteristics. Additionally, they are able to clarify and solve occurring problems and are able to bring the involving sectors closer together (Yukl, 2012). Especially in OH initiatives, leadership must facilitate collective learning, advocate change and encourage innovation to tackle complex health problems (Rüegg et al., 2018a).

As different sectors are involved in a OH initiative, it is essential not to focus on one operational leader but on shared and equal leadership involving all sectors and disciplines as one dominating discipline would be detrimental for cooperation and commitment. With shared leadership, the capacities of involved sectors can be used optimally and mutual forms of influence take place which has in turn a positive effect on the cohesion between sectors (Houghton et al., 2015).

This assessment tool will help to evaluate teamwork and interdisciplinarity throughout the initiative. Suitable team play, change-oriented leadership skills, and clear competences and goals receive a high score on OH systemic organisation (Rüegg et al., 2018b).

4.1.2 Data collection tools/ data sources

The framework for the evaluation of OH proposed by the NEOH has been used as a guidance throughout the entire study. To ensure reliable results, it was important that the evaluation of the CYSTISTOP project was performed by an unbiased objective person.

Data sources for elements 1 and 2, consisted of available literature, personal communication and the CYSTISTOP protocol. To quantitatively assess the OH-ness of CYSTISTOP in element 3, questionnaires were formulated and administered according to the fill-in Microsoft Excel spread sheet developed by the NEOH. The questionnaire was set up in a PDF document and adjusted to suit this initiative. Since the participants had different functions within the initiative, such as PhD- students, it could not be expected that they would be able to answer the complex questions about the design of the initiative. Therefore, an adapted questionnaire was used in which several questions primarily regarding the initial planning were omitted, referred to as the ‘non-core group questionnaire’ and included 47 multiple choice questions. The questionnaire addressed to the stakeholders who were additionally involved in the designing and planning of the initiative is referred to as the ‘core group questionnaire’ and involved 54 multiple choice questions (appendix II).

Data sources for element 4 consisted of the outcomes of the OH-ness of CYSTISTOP obtained in element 3 and available reported outcomes of the intervention studies in Zambia.

4.1.3 Data collection

As described by the NEOH, data for element 3 was collected with the use of structured semi open interviews along with the use of available literature on the initiative. To gain full insight on the different aspects and multidisciplinarity of this study, project members with different fields of interest and responsibilities within CYSTISTOP needed to be involved and interviewed. Stakeholders were identified as individuals directly involved in the design of the project and field interventions, and included a scientific study advisor, the study coordinator and co-promotor, both principal investigators on the veterinary and medical part and PhD students. Stakeholders were contacted via email with the invitation to participate in the assessment of CYSTISTOP’s OH-ness via an online interview and questionnaire.

If consent was given, the questionnaire was sent to the stakeholder a few days before the interview started. All interviews were conducted in the same way following a protocol (see Appendix I) via Microsoft Teams videocall and lasted approximately 1 hour. After permission, the interviews were recorded within the Microsoft Teams application. During the interview, results were noted on the printed version of the questionnaire and were subsequently entered into Google Forms directly after ending the interview. This facilitated calculating the average scores for each question and enabled entering the scores in the NEOH Excel tool.

4.1.4 Data analysis

To analyse the collected literature to complete elements 1 and 2, specific information about the context of the initiative and design of the initiative were sought. Elements 1 and 2 were important preceding descriptive elements to gain insight on the initiative which permitted to analyse the obtained OH-ness data in element 3 and to assess element 4.

Obtained data for element 3 was quantitatively analysed using the obtained average scores given by the interviewees in the questionnaire. These questions were each to be scored from 0 to 1 according to the participant's answers. Assigned scores close to 1 represent a high degree of realization of the different OH characteristics. Each question was given the same weight, excluding the learning assessment where the weight depended on the degree of influence on institutional learning. To obtain the final score for each question, an average of all the answers given was calculated and was rounded at 2 decimals after the comma. The obtained scores were entered in the corresponding criterion in the Excel tool. Subsequently the median scores, per OH assessment tool, were automatically calculated (thinking, planning, working, sharing, learning and systemic organisation). A visual representation of the Excel tool is provided in Figure 7.

No.	Evaluation elements/questions	Short element description/explanation	Reasoning behind the score for the element / qualitative assessment	Score	Scoring guidance
1	Common aim(s) in initiative	Is/was the initiative planned to aim for a common overarching cross-sectoral and -disciplinary goal relevant to One Health including health, societal, environmental and/ or economic outcomes (sustainable solutions)?			0=no common OH-relevant aim(s) 0.2=few/little common OH-relevant aim(s) 0.4=some common OH-relevant aim(s) 0.6=common and OH relevant aim(s) 0.8=highly common and OH relevant aim(s) 1=clear common and fully OH relevant aim(s)
2	Planned organisation needed to reach common aim(s)?	Is/was the planned organisation in terms of staff positions and involvement, participating institutions, networks, communication pathways, leadership etc. of the initiative relevant and needed to achieve the stated aim(s) (i.e. is a One Health approach supported?)			0=organisation not supportive of OH approach 0.2=organisation slightly supportive of OH approach 0.4=organisation somewhat supportive of OH approach 0.6=organisation supportive of OH approach 0.8=organisation highly supportive of OH approach 1=organisation fully supportive of OH approach
3	Stakeholder* identification process ('the right people heard'?)	Has a process to identify and engage all essential stakeholders (e.g. governmental, academia, industry, NGOs, general population, etc.) been used in the planning of the initiative?			0=no identification process 0.2= minor identification process 0.4= identification process partly used 0.6= reasonable identification process used 0.8= highly relevant identification process used 1= perfect identification process used
4	Actor** identification process ('the right people involved'?)	Has a process to identify and involve essential actors (including governmental, industry, health units, professionals, technicians, etc.) been described and followed in the planning of the initiative?			0=no identification process 0.2= minor identification process 0.4= identification process partly used 0.6= reasonable identification process used 0.8= highly relevant identification process used 1= perfect identification process used

Figure 7. An example of the criteria used to assess the OH-ness in element 3, using the Microsoft-Excel-spread sheet developed by the NEOH.

Visualisation on the balance of each assessment tool was provided via a spider diagram in the Excel tool which is presented in Figure 8. The spider diagram stressed the strengths and weaknesses of each domain.

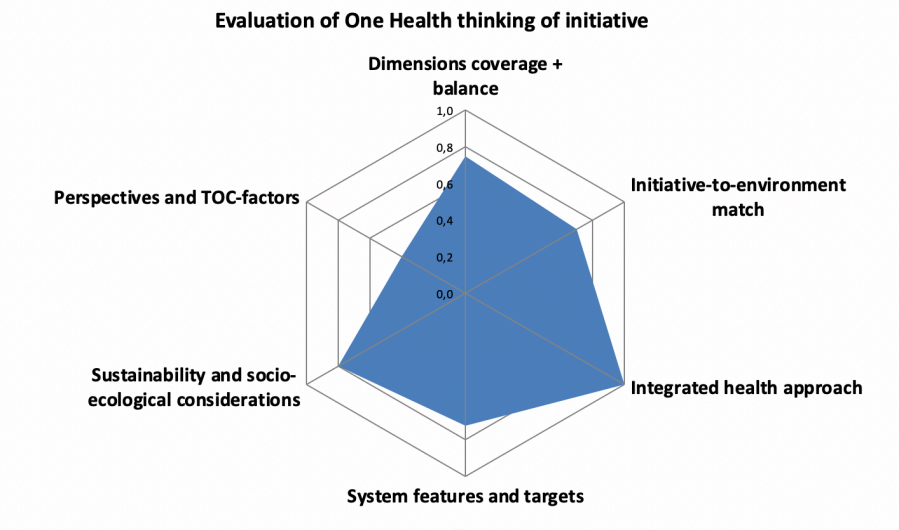

Figure 8. Spider diagram of a fictive initiative's One Health thinking processes

Subsequently the OHR and OHI were automatically calculated once all scores for the assessment tools were obtained. The formulas used to calculate the OHI and OHR were the following:

$$OHI = \frac{\{(ScP \times ScT)+(ScL \times ScP)+(ScS \times ScL)+(ScO \times ScS)+(ScW \times ScO)+(ScT \times ScW)\}}{6}$$

$$OHR = \frac{\left(\frac{ScO \times ScW^2}{ScO+ScW}\right)+(ScW \times ScT)+(ScT \times ScP)+\left(\frac{ScP^2 \times ScL}{ScP+ScL}\right)}{\left(\frac{ScP \times ScL^2}{ScP+ScL}\right)+(ScL \times ScS)+(ScS \times ScO)+\left(\frac{ScO^2 \times ScW}{ScO+ScW}\right)}$$

ScT: thinking
ScP: planning
ScW: working
ScS: sharing
ScL: learning
ScO: systemic organisation

Data for element 4 was analysed through the comparison of the degree of OH-ness of the initiative obtained in element 3 and the achieved outcomes by the initiative described in published reports.

5. Results

5.1.1 Element 1: The definition of the initiative and its context

5.1.1.1 Description of the One Health initiative

T. solium is endemic in most countries of SSA leading to major human health- and economic consequences. Although some interventions and control programs have been carried out in the past, they have never succeeded in eliminating the parasite. These interventions had the implementation of stand-alone control options in common which were proven ineffective in eliminating *T. solium* in the longer term. Better outcomes might be achieved by the implementation of more integrated or prolonged measures. However, this had never been studied before in SSA (de Coster et al., 2018).

To fill in this gap, CYSTISTOP, a pilot study, was established to determine the best way forward for *T. solium* control and elimination in SSA. The outcomes of this initiative will contribute to the future strategy as the study will indicate whether a short-term elimination program or a long-term control program, with potential for elimination in the future, will provide the best possible and achievable results for SSA (Gabriel et al., 2016).

CYSTISTOP is an interdisciplinary collaboration between the Institute of Tropical Medicine, Antwerp; Ghent University, Faculty of Veterinary Medicine; Université catholique de Louvain, Faculty of Public Health; Scientific Institute of Public Health; University of Zambia, School of Veterinary Medicine, Zambian Ministry of Health; Ross University School of Veterinary Medicine; University of Florida. Funding of the study is provided by the Flemish Ministry of Research, Institute of Tropical Medicine, Antwerp (SOFI) and GALVMED.[16]

As illustrated in the following paragraphs, the most important drivers for this initiative can be identified as the massive burden of *T. solium* neurocysticercosis on human health and mental wellbeing, costs due to health problems and required health care, economic consequences for pig farmers and the lack of research into which strategies are most cost-effective, acceptable and feasible in SSA conditions.

A community-based study in Katete pointed out that 11,9% of people sampled, tested with a copro-Ag-ELISA, were carriers of the tapeworm. This finding suggests that high degree of environmental contamination with *T. solium* eggs takes place which greatly increases the chance of humans and pigs acquiring neurocysticercosis and porcine cysticercosis, respectively (Mwape et al., 2013). A research on the prevalence of epilepsy due to neurocysticercosis in this area pointed out that more than half (57,1%) of epilepsy was caused by neurocysticercosis (Mwape et al., 2015).

Although the exact socioeconomic costs of *T.* solium in Zambia are unknown, a preliminary cost estimation study conducted in Zambia showed that the parasite significantly affects the economic status of people and communities (Hobbs et al., 2018). Seeking medical help itself is free in Zambia (on the level of the patient), however many indirect costs are associated with the parasite. Indirect costs related to symptomatic patients suffering from neurocysticercosis include also incapacity to work and loss of productivity, losing their job, hospitalization costs and time for transport to seek medical care. In addition, there are economic losses for pig keepers as animals identified as infected, after tongue palpation, are sold with a value loss of 45% compared to healthy animals (Hobbs et al., 2018).

In addition, neurocysticercosis significantly affects mental wellbeing as in certain cultures, there is still a lot of ignorance of medical conditions that can cause epilepsy. Epilepsy is often attributed to mystical events, punishment for sins or witchcraft. As a result there is a lot of stigma with massive impact on the social and economic status of patients suffering from epilepsy (Winkler et al., 2010). A study by Birbeck et al. found that people in Zambia with epilepsy have a significant poorer social and economic status in comparison with people suffering from other medical conditions. Other consequences resulting from the stigmatization of epilepsy are reduced employment status, decreased education, suboptimal housing and - environmental quality and higher food insecurity (Birbeck et al., 2007).

These findings stress the importance of finding sustainable control or elimination measures.

The specific objectives of CYSTISTOP were to verify whether an integrated approach is effective under African conditions, what the costs and cost-efficiency of both control and elimination options were, how the local communities would feel about the proposed program, whether there would be any added value and what that would be of an elimination program compared to a control strategy. In addition, the initiative wanted to investigate what the economic consequences of *T. solium* were on the society and community; on pig farming, both on individual and societal level and to what extent health education (via computerized systems) had an influence on the knowledge and behaviour of school-going children.

[16] https://www.ugent.be/di/vph/en/research/fpz/projects/taeniasolium2

Several areas in the Eastern province had potential to participate in the study. The Katete district was chosen as study region based on various factors. Since CYSTISTOP's proposers had previously conducted several studies in the area, large amounts of data were already collected and there was experience with working in this area. Other factors that led to the choice of the region were the endemicity rate of *T. solium,* willingness of the community to participate, accessibility of roads, proximity of rural health centers, and the degree of isolation communities towards others (Gabriel et al., 2016).

The objectives were addressed in 5 work packages, spread over 7 years. The study consisted of an elimination, control and negative study arm (Gabriel et al., 2016).

In Work package 1 a systematic review of the available literature was conducted. This facilitated the selection of potential intervention measures with the most promise according to local acceptability and cost effectiveness. Work package 1 was completed in the first year of the study (Gabriel et al., 2016).

As mentioned in previous paragraphs, studies on prevalence of neurocysticercosis, cysticercosis and taeniosis had already been conducted in Katete. The results from these studies provided valuable data for CYSTISTOP. **Work package 2** included the adjustment of the disease transmission model for *T. solium* under expected Zambian conditions. The model provided guidance on the type and frequency of intervention to achieve elimination or control. Subsequently, the modelled elimination and control interventions were graded for suitability under Zambian conditions for each of the study arms and were assigned thereafter. As described in CYSTISTOP protocol, the researchers took into account that a disease transmission model is based on assumptions and might not represent reality. Therefore, the disease transmission model was updated throughout the duration of the project as soon as the results of the interventional field studies became available (Gabriel et al., 2016).

Work package 3 started in the second year of the study and included the interventional field study and the collection of quantitative biomedical data. The study consisted of three study arms; an elimination, control and negative study arm which were carried out in 3 separate study communities. The elimination study arm combined human mass drug administration and health education. Pigs received oral drug administration and vaccination. The control intervention study arm implemented health education and drug administration in pigs. Lastly, the negative study arm had no implementation of a specific intervention, though some health education was implemented for ethical reasons.
Pigs and humans were sampled at pre-determined times to determine the course and outcomes of the intervention. The primary outcome of the elimination study arm was porcine cysticercosis, secondary outcomes were taeniosis and human cysticercosis. In these study arms, the short-term elimination of *T. solium* via integrated measures involving pigs and humans was compared with a long-term control strategy that solely considered pig-related measures (Gabriel et al., 2016).

In work package 4 socioeconomic data collection and assessment took place from the first year until the end of the study. Questionnaires and focus group discussions were conducted in the local control and elimination communities by trained survey personnel to assess the impact of *T. solium* on their social and economic well-being and the acceptance of the interventions. Additionally, a socio-economic evaluation and follow-up was carried out regarding the intervention field studies (Gabriel et al., 2016).

Work package 5 focused on sharing and reporting the results of the study both internally as externally throughout the duration of the project (Gabriel et al., 2016).

5.1.1.2 Description of the context of the initiative

There are several reasons why the endemicity of *T. solium* in Zambia is so high. Human behavior and certain cultural groundings are key factor in the transmission cycle of *T. solium* in Zambia. In rural areas, open defecation is the norm although latrines are present. Reluctance of latrine use has social-cultural groundings. For example, there is a taboo against accidentally meeting in-laws, parents or children in the toilets. In addition, toilets can be poorly constructed which can startle children and provide poor privacy (Thys et al., 2015). Besides the fact that open defecation is a major risk factor for the spread of

T. solium eggs, free range pig management is another major risk factor. These 2 practices are both standard practices in these rural communities which enhances the transmission cycle of *T. solium* as free ranging pigs can easily come into contact with *T. solium* eggs. The main reason reported for free roaming pig management is feed shortage. As families often experience food insecurity, regularly feeding confined pigs can be difficult. Free roaming pigs on the other hand can find food by scavenging (Thys et al., 2016).

Most pigs are slaughtered in backyard conditions, whereafter meat is sold from door-to-door resulting in a lack of meat inspection and infected meat entering the food chain. Additionally, there is a shortage of meat inspectors in slaughter facilities. Since meat is a valuable source of protein and there is often no knowledge of the dangers of infected pork, contaminated meat is not rejected, but sold at lower prices or used for personal consumption (Thys et al., 2016).

Lack of knowledge among villagers and rural physicians and veterinarians, and low treatment rates of people infected with *T. solium* are also key factors. Poor hygiene practices in meal preparation and certain habits whereby meat is roasted are sources of acquiring taeniosis as cysts remain viable. For example, it is reported that especially beer drinking men tend to consume undercooked pork and cysts in meat are reported to be enjoyed as it creates a certain sensation when consumed. Cysts are believed to develop as a result of corn eaten by pigs. Consequently, contaminated meat can be even more demanded and expansive than noninfected meat (Hobbs et al., 2020; Thys et al., 2016).

5.1.1.3 Description of the initiative in its context

The stakeholders and actors affecting the initiative are scientific researchers, scientific/public health institutes, doctors, veterinarians, nurses, trained survey personnel and laboratory practitioners. The initiative affects the local communities (at the level of health, knowledge, economy, and the food system), animals (pigs), the government and policymakers (as information about the best way forward is provided). In addition, other researchers are informed by the obtained results and knowledge. Figure 9 provides a visual representation of the context of the system and the impact of CYSTISTOP.

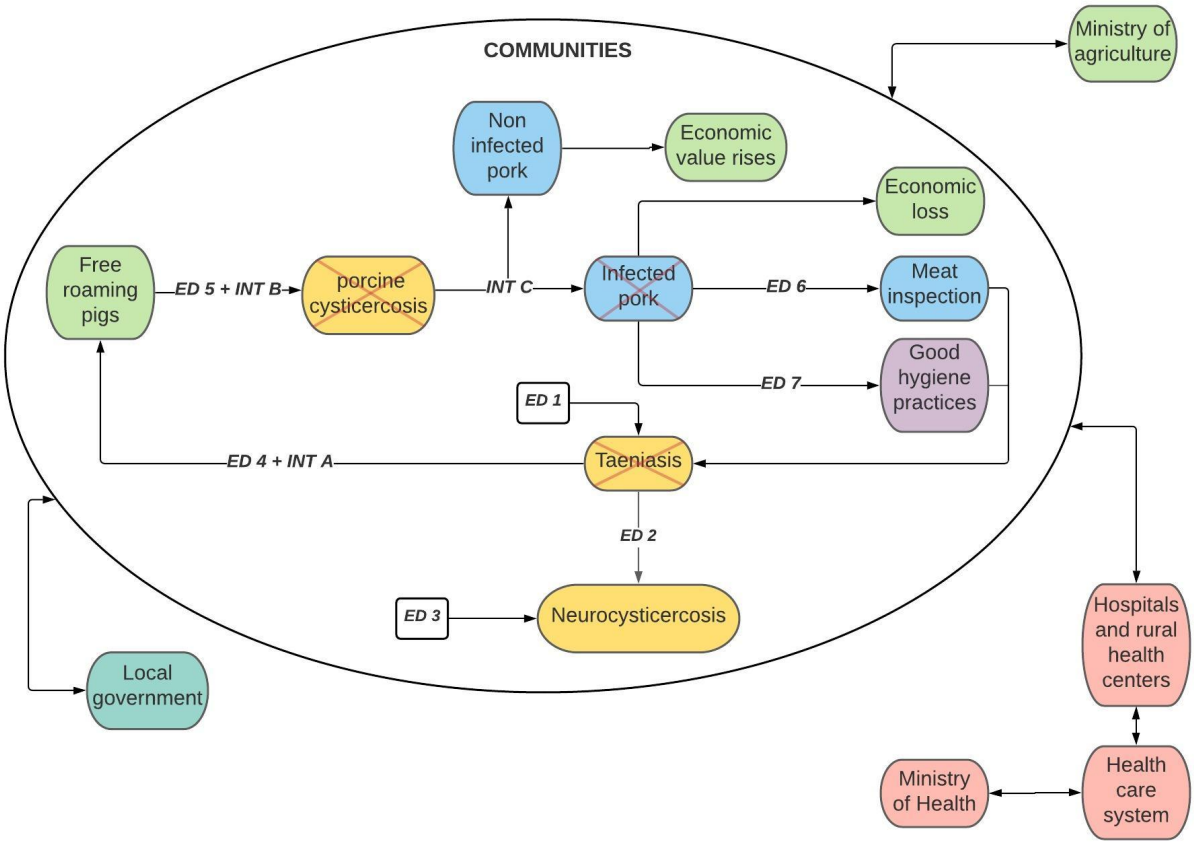

Figure 9. A visual representation of CYSTISTOP within its context. Arrows marked with education (ED)/ intervention (INT) represent education or intervention to break the T. solium life cycle on a local scale. Double pointed arrows imply the impact of CYSTISTOP on the food system (green), on health care (red) and on the local government (dark green) through providing findings and data of the outcomes of the study. A red cross indicates breaking the cycle by prevention/treatment of disease. ED 1: education on self-diagnosis and importance of medical care; ED2: education to prevent intake of T. solium eggs and hygiene; ED3: education on seeking treatment for neurocysticercosis; ED4: education on hygiene to prevent eggs from entering the environment via open defecation methods; ED5: education on the importance of pig confinement; ED6: education to stress the importance of meat inspection; ED7: Education on good hygiene practices e.g. cooking meat and clean water. INT A: treatment of people with taeniosis; INT B: vaccination of pigs; INT C: mass drug administration.

Essential to find sustainable measures to tackle *T. solium* is taking several aspects of the transmission cycle into account. CYSTISTOP responds to the principles of an interdisciplinary approach and takes the complex socio-cultural-economic system, highlighted in section 5.1.1.2, associated with *T. solium* in account. The initiative acts upon various patterns in disease transmission as intervention strategies target several subsystems and it takes the chain of events contributing to disease occurrence into account.

Education plays an important role in the elimination and control study arm. With the use of educational tools, e.g. 'The Vicious Worm' an interactive tool used in school going children, specific cultural risk-habits are addressed. Therefore, knowledge is increased, which improves hygiene practices (latrine use, cooking meat, washing vegetables) and reduces chance of infection. People are additionally educated on infection and transmission routes, methods for self-detection of tapeworm infection and the importance of seeking medical care in rural health centers and hospitals (Gabriel et al., 2016).

CYSTISTOP does not only focus on health outcomes as economic aspects are also important in this study. The economic situation of pig keepers and non-pig keepers is investigated, and related costs are calculated from a community and governmental point of view. In addition, the cost-effectiveness of the various interventions is calculated, which contributes to persuade and inform policymaker and funding to later implement intervention measures on a larger scale.

As pig health improves, the quality of pork and consequently the price will increase, leading to more income for communities that rely mainly on pig farming as a source of income.

The initiative contributes to animal health as the rate of infected animals will decrease. The impact of education might also lead to the animals being housed more intensively to avoid infection which increases monitoring of other health related aspects. In addition, contact with other animals can be more intensively monitored which might reduce the transmission of pathogens between different herds.

There are boundaries for interventions aiming to reduce *T. solium* endemicity in Zambian conditions. A first limitation is the existing socio-cultural-economic system inherent to the rural areas of Zambia/SSA. Precisely because certain behaviors represent an increased risk of passing on infection/ acquiring infection, responding to this system is important. However, these systems have existed for decades, provoking change can be difficult to achieve, and change might not be accepted. Therefore, CYSTISTOP tested the local acceptability of the communities and integrated education in its control and elimination study arm. Although education might raise awareness and can provoke change in people's behavior, it is a very gradual process that requires a long time of change and persistence as certain behaviors are deeply rooted in these communities. This is an important boundary to consider, especially when suitable control and elimination measures will be applied at higher scale in the future.

A limitation of CYSTISTOP is that the initiative is conducted in 'ideal' circumstances, with regard to infrastructure and willingness of the communities to cooperate. Although intervention measures might be feasible and acceptable for these involved communities, this can be different in other SSA countries. This can make implementation of the proven suitable intervention measures on a large scale in the future more difficult.

Another limitation is the fact that the life cycle of the parasite can be hard to understand for people in these communities, especially without scientific background. A lack of understanding can make participants less cooperative and more suspicious to participate in certain interventions.

5.1.2 Element 2: The description of the Theory of Change

Complementary to a OH initiative, the overarching outcomes of CYSTISTOP are health and welfare of humans, animals with regard to the environment managed by integrated health strategies. Before discussing how the initiative intends to produce its expected outcomes, the expected outcomes themselves will be described.

The desired outcomes, and essential aspects for progress towards long-term goals, that wanted to be demonstrated at the end of the study were the following:

The CYSTISTOP project wanted to demonstrate that elimination of *T. solium* was possible under SSA conditions and that control and elimination options had a significant impact on the disease occurrence. Other desired outcomes were that integrated measures had a greater impact than single control options, the use of the educational tool 'The Vicious Worm' had a positive influence on the knowledge of school-aged children, and that the local acceptability of several control and elimination options in communities, endemic for *T. solium,* depends on several factors and is therefore not the same in every community. In addition, the socioeconomic impact of *T. solium* on local communities from a community and governmental point of view was assessed and information on the costs and cost-effectiveness of the applied interventions would be provided (Gabriel et al., 2016).

The process of CYSTISTOP to produce its outcomes and the long-term goals are described in section 5.1.1.1 and are illustrated in Figure 10.

These steps all lead to the main goal of this pilot study; to find sustainable control and elimination options to tackle *T. solium* in SSA and to assess their cost-effectiveness and local acceptability. These outcomes generated by CYSTISTOP result in more suitable intervention strategies and provide valuable

information on cost-effectiveness will help to inform and persuade policymakers and funding bodies to conduct interventions in the future, and potentially on a larger scale. These solutions can have major impact on many affected communities as the prevalence of neurocysticercosis will decrease and human health will improve. This aids the economy as a healthy community is more productive and reduced health care costs are beneficial for governments. Education can reduce stigma, raising awareness of the importance of infectious and non-infectious (zoonotic-) diseases for health, also regarding other diseases.

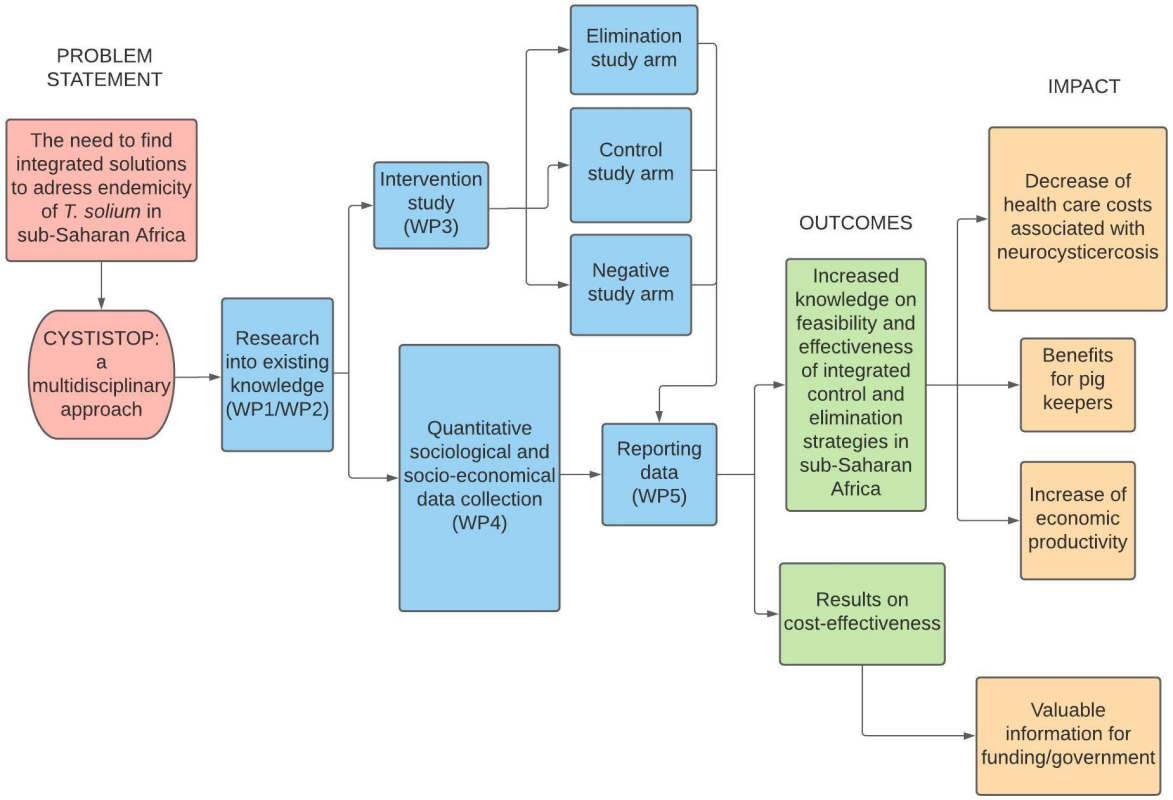

Figure 10. The initiative's Theory of Change: the pathway and building blocks needed to reach its objectives and to produce the desired outcomes. Blue boxes refer to the building blocks used within CYSTISTOP. Green boxes refer to the direct outcomes of the initiative and orange boxes refer to the impact of the long-term of the outcomes of the initiative.

The initiative took unexpected outcomes into account in its TOC, as many problems can arise during working in field-circumstances. The initiative was prepared to respond to these problems, seeking the best possible solutions. This is further addressed in element 3.

5.1.3 Element 3: The process evaluation of operational and supporting infrastructures

5.1.3.1.1 One Health thinking

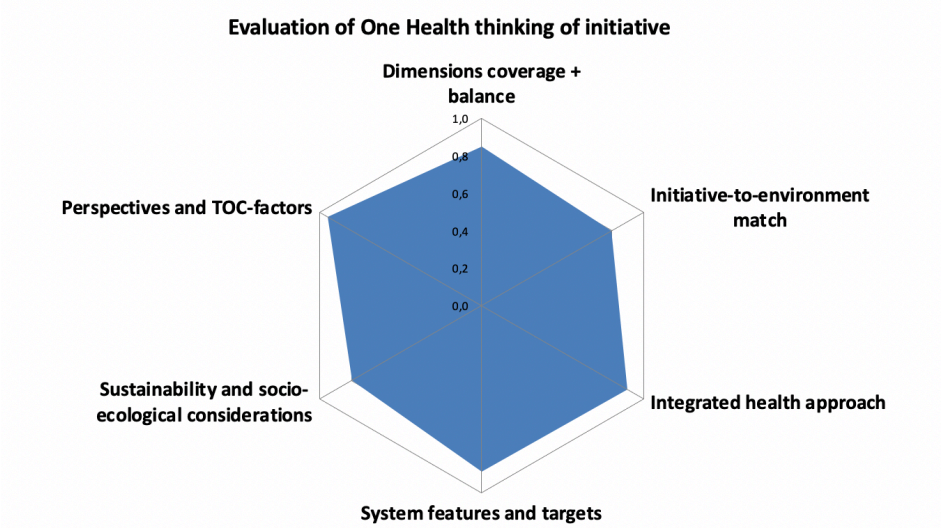

Figure 11. Spider diagram of the initiative's One Health thinking processes. The obtained scores were: dimensions coverage + balance (0,8); initiative-to-environment match (0,8); Integrated health approach (0,9); systems features and targets (0,89); Sustainability and socio-ecological considerations (0,8); Perspectives and TOC-factors (0,95).

The results obtained for OH thinking are demonstrated in Figure 11. As a result of the need for effective strategies and an integrated approach, the initiative automatically focused on both disciplines of human and animal health, with the characterization of societal, environmental and economic factors. As the area where CYSTISTOP was carried out was well considered, the initiative fitted well into its context. Therefore, a score of 0,8 is obtained for 'initiative-to-environment match'. CYSTISTOP actively involved multiple important dimensions, scales and subsystems of the context important to the system in which it operated which is reflected by the score of 0,8 obtained for 'dimensions coverage and balance' and 0,9 for 'integrated health approach'.

Within 'system features and targets', the situation of the initiative in relation to the chain of events causing the problem it wants to respond to, time analysis and the use of feedback loops was assessed. With detailed knowledge on disease transmission patterns and on the importance of human behaviour with regard to the transmission cycle, CYSTISTOP took different stages of the chain of events of the life cycle and transmission routes of the parasite into account. In order to set up the three different study arms, the initiative had to use causal connections and think at structural level to achieve its aims. In addition, social systems were recognised and social scientists were involved as willingness of the communities to participate was decisive for the initiative's feasibility. The implementation of education in all study arms allowed the initiative to modify the socio-ecological system towards sustainability in some extent. A detailed time analysis was worked out regarding the optimal timing and intervals of interventions and sampling. In addition, delays and unforeseen circumstances due to field work were considered and delays for the approval for ethical clearance were precalculated. However, the initiative did not anticipate on large time delays during the initiative itself, e.g. COVID19, and these were subsequently not recognised in the TOC. In the early stages of designing the project, a high degree of feedback and action was considered. All these aspects contribute to the score of 0,89 obtained for 'system features and targets'.

As the initiative aims to find sustainable solutions, whereby society, environment and economy are taken into account with the use of integration of disciplines, the score obtained for sustainability and socio-ecological considerations is 0,8.

The initiative obtained a nearly perfect score of 0,95 for 'perspectives and TOC factors' as experience and perspective of the stakeholders were important in providing the backbone of the initiative. Stakeholder involvement stemmed from previous collaborations causing stakeholder views and opinions to be highly relevant. Since previous conducted intervention studies in SSA were ineffective, beliefs about evidence and values about cultural grounding were important factors considered by the initiative and applied in the initiative's TOC.

The overall score obtained for OH thinking is 0,80.

5.1.3.1.2 One Health planning

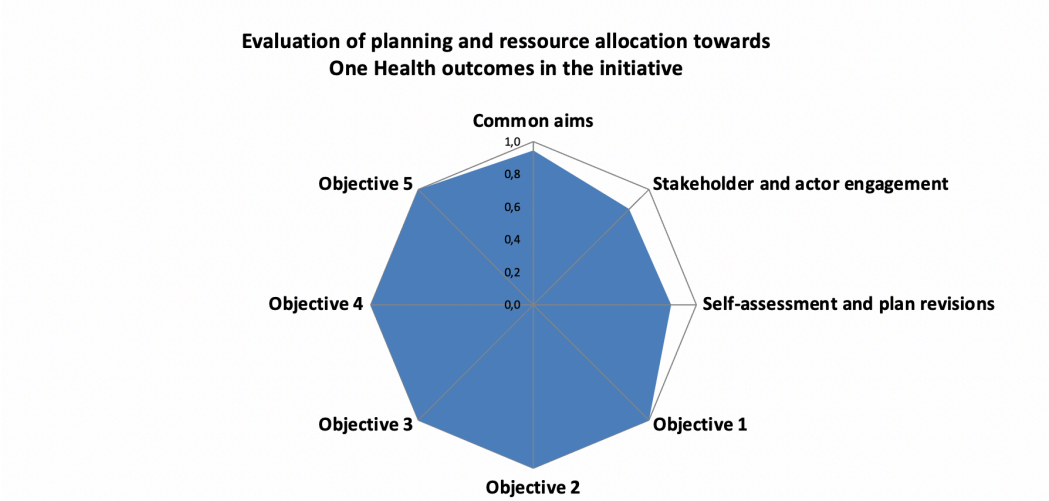

Figure 12. Spider diagram on the initiative's One Health planning processes. The obtained scores were: Common aims (0,9); Stakeholder and actor engagement (0,8); Self-assessment and plan revisions (0,8); Objective 1 - 5 (1).

The results obtained for OH planning are demonstrated in Figure 12. As this pilot study implements field interventions in a clinical trial setting, all objectives had to be planned perfectly, and resources needed to be allocated in order to successfully complete them, therefore all objectives were scored with 1.

Common aims of involved stakeholders and disciplines were essential in this initiative. In addition, the planning was highly supportive of a OH approach, as the initiative took into consideration that both medical and veterinary stakeholders were essential to this initiative. However, as the environmental sector was not fully engaged, the initiative was not fully supportive of an OH approach. These findings are supported by the score of 0,9 obtained for 'common aims'.

No specific identification process was used to identify important stakeholders. As previously mentioned, this project stemmed from stakeholders who previously collaborated meaning that there was no specific need to implement a perfect identification process in the planning of the initiative. However, actor engagement was really important to conduct field interventions. Therefore, actor identification did occur thoroughly to ensure the involvement of the right actors (nurses, local health centres, laboratory workers) However, these people were not identified in person in the planning part yet as the nurses that would join the intervention teams were depending on who was available at that time. At proposal stage, there was a high degree of engagement of different stakeholders in the planning of the initiative especially stakeholders at top level. These stakeholders include the Institute of Tropical Medicine, University of Zambia, and the Zambian Ministry of Health. During later implementation, a few more people that were active on a lower level in the initiative e.g. vets, physicians and people related to the Ministry of Health, became involved in further planning aspects as well. However, not all actors were involved in the planning part of the initiative i.e. nurses that worked at the rural health centre were not involved in the planning as there was no specific need to. These results lead to a score of 0,8 was regarding the assessment of 'stakeholder and actor engagement'.

Stakeholder perceptions, feedback and input were perceived as very important in this initiative and were highly taken into account. In addition, the initiative anticipated in the planning part on problems that might occur during the implementation of field activities, making sure they were ready and flexible to respond to these problems. This facilitated making feasible adjustments where needed and to help overcome problems in the initial stages of the initiative. As a result, CYSTISTOP is based on an iterative process, in which consideration was given to what outcomes might be achieved and what implementation was feasible. Although, the initiative used a high degree of self-assessment to revisit, there was not formally time nor budget allocated to do so in the initial planning stages of the initiative which reduces the overall score when scored according to the NEOH framework. However, self-assessment became self-evident for the initiative as it evolved, and budget was not necessarily needed to do so. The score for 'self-assessment and plan revisions' is consequently 0,8.

The overall score obtained for OH planning is 0,98.

5.1.3.1.3 One Health working

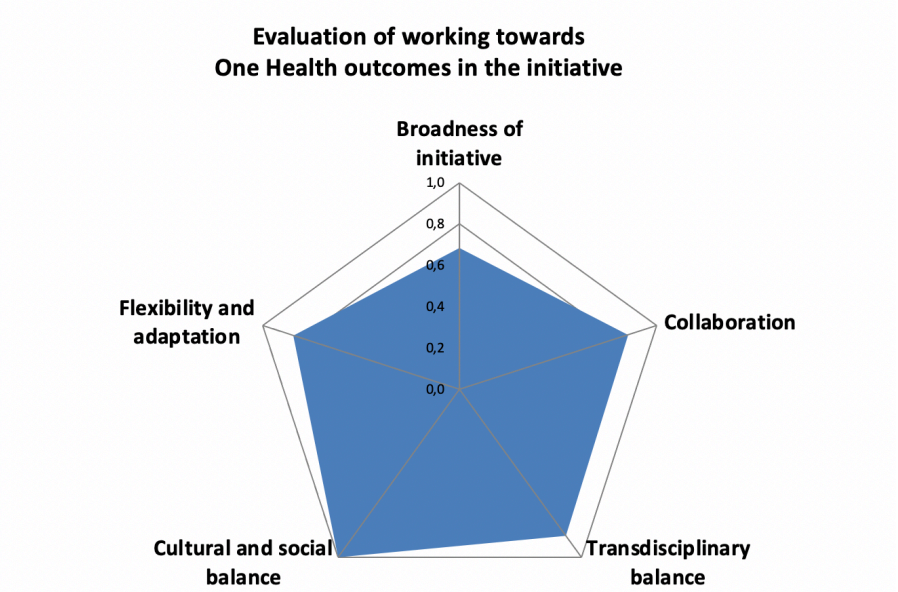

Figure 13. Spider diagram on the initiative's One Health working processes. The obtained scores were: broadness of initiative (0,7); collaboration (0,9); transdisciplinary balance (0,9); cultural and social balance (1); flexibility and adaptation (0,8).

The results obtained for OH working are demonstrated in Figure 13. With a score of 0,7, broadness of the initiative scored less compared to the other criteria for OH working. Indeed, the environmental sector could have been much more involved within CYSTISTOP as this sector is mainly part of the education process. However, to achieve the initiative's stated aims and objectives the degree of involvement did suffice. Although the community itself was extremely involved in the intervention studies when it comes to acceptability, no decision making took place from within the communities themselves. However, this criterion might not be relevant within this initiative, but it contributes to a OH approach within terms of 'broadness'.

The initiative obtained a score of 0,9 for collaboration. Meetings with all disciplines were held as frequently as possible. However, as CYSTISTOP involved stakeholders from different countries which were additionally involved in other ongoing projects, this was not always self-evident. As interventions, involving all disciplines, in the beginning of the initiative took place every 4 months there were at least 3 planned meetings a year. In more recent years, meetings were held twice a year. Although meetings with all disciplines involved were not held as frequent, stakeholders reported that there was regular

spontaneous interaction in between the interventions via email/ videocall and additionally face-to-face between stakeholders that lived in the same area to foster collaboration.

The implementation of an interdisciplinary approach was highly relevant for this initiative as stand-alone options had proven to be ineffective. Even though the head coordinator and stakeholders who mainly designed the program were veterinarians, no specific inequality between the involved disciplines and sectors in further implementation had been reported. A strength of this initiative is that it relied solely on joint decision making between the involved disciplines, which ultimately adds on to a OH approach. Therefore, a score of 0,9 on 'transdisciplinary balance' is obtained. In addition, there were no reports on inequality between stakeholders based on function, gender, ethnicity, religion or cultural issues. Consequently, the initiative scored perfect on 'cultural and social balance'.

The score obtained for 'flexibility and adaptation' is 0,8. As CYSTISTOP is a scientific research (clinical trial), major changes in the project design could not be implemented without affecting the entire program. In addition, the interventions at the beginning of the program were mostly fixed as intervals between human/animal treatments had to be predetermined. Therefore, the project design could not respond to major internal/external changes at short-term. However, the project was designed flexible to respond to internal/external changes at mid- and long-term as it was already clear in the thinking and planning stages that adjustments were likely to be made. For example, feedback of the non-scientific community was extremely important for this initiative as local acceptability of intervention measures had to be determined. When field practices did not work out, advice was sought by the local leaders and field assistants who advised the stakeholders. Consequently, action was taken based on received feedback. Other unexpected changes that the project had to respond to were outbreaks of African Swine Fever (ASF). Due to major pig loss, the project had to react flexible to this event and adjustments in the number of pigs that needed to be sampled were made.

The overall score obtained for OH working is 0,88.

5.1.3.1.4 One Health sharing

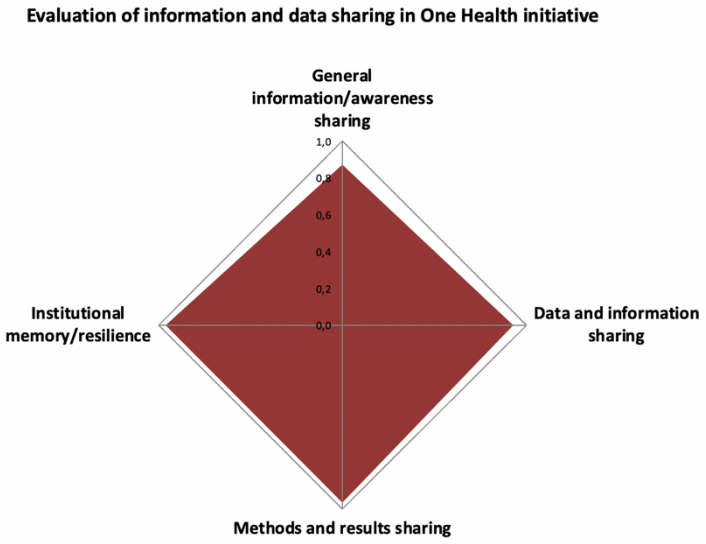

Figure 14. Spider diagram on the initiative's One Health sharing processes. The obtained scores are: general information/awareness sharing (0,87); data and information sharing (0,93); methods and results sharing (0,96); institutional memory/resilience (0,96).

The results obtained for OH sharing are demonstrated in Figure 14. Internal mechanisms to share results were reported to be present and used on a regularly basis. Reports were available, and results were published between stakeholders within the initiative. In addition, the initiative presented its progress at conferences, both locally and internationally and results were published external on a

regularly basis. All collected data was shared on Google Drive, which made data easily accessible and available for the interested stakeholders. Smartphones and tablets were allocated by the initiative for mobile data input and collection. Based on these outcomes, the score for 'general information/awareness sharing' is 0,87.

Data was fully and always shared between disciplines after every intervention, and in addition daily when needed. Formal agreements were made concerning data sharing and collected data was available for all interested stakeholders on the Google Drive. There was a large investment to provide quality data, with a strong focus on error checking and the use of back-ups. In addition, the initiative took into account that the duration of the initiative would be several years and that stakeholders could leave the project or switch positions. Therefore, to avoid data loss, attention had been paid to data storage. As the initiative did really think these aspects through, 'data and information sharing' is scored as 0,93.

Methods and results were fully shared between the relevant stakeholders and disciplines in the initiative. The veterinarians were fully aware of the objectives, methods, results obtained by the medical doctors and vice versa. Therefore, a score of 0,96 is obtained for 'methods and results sharing'.

Institutional knowledge reservoirs were created, as results were often published, and several PhD students were involved in the program. In addition, mechanisms were put in place by the initiative to safeguard data, information and results. This reflects a high degree of 'institutional memory and resilience' with an obtained score of 0,96.

The overall score obtained for OH sharing is 0,93.

5.1.3.1.5 One Health learning

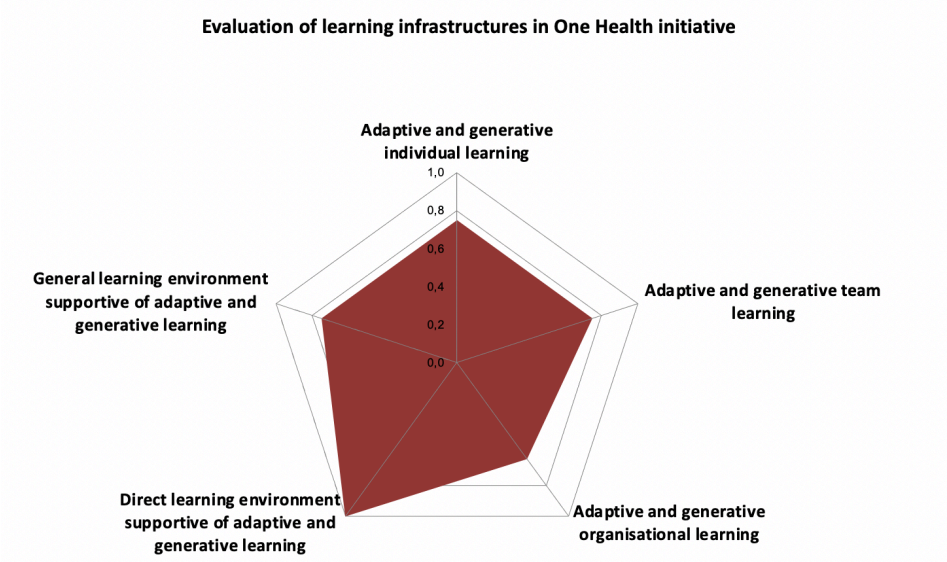

Figure 15. Spider diagram on the initiative's One Health learning processes. The obtained scores were: Adaptive and generative individual learning (0,75); Adaptive and generative team learning (0,75); Adaptive and generative organisational learning (0,63); Direct learning environment supportive of adaptive and generative learning (1); General learning environment supportive of adaptive and generative learning (0,75).

The results obtained for OH learning are demonstrated in Figure 15. Within 'individual learning' there was a clear difference between the answers given by interviewees based on their experience with these intervention studies. The average answer for individual learning was that it occurred 'very often'. Stakeholders that had less experience with intervention studies were more likely to reply that received information was put into practice outside of the initiative and that it improved their competencies very often. Stakeholders who had been involved in intervention studies a lot more often, were more likely to reply that individual learning happened sometimes. This can be explained by the fact that these

experienced stakeholders already have a certain degree of competence and knowledge and stresses the added value of the initiative on individual learning of less experienced stakeholders. The obtained score for ‘adaptive and generative individual learning’ is 0,75.

‘Generative team learning’ scored 0,75. Often reported by the interviewees was the appreciation towards teamwork and the fact that everybody’s opinion was taken on board. This interaction did help to create new views and ideas which permitted working towards new projects. As a result, other projects evolved from this initiative e.g. the SOLID project.

Existing knowledge and information about the context of the initiative was stored within the initiative and collected information was very often discussed at various levels within the organisation. Sharing information and discussing did lead to changing some ideas and approaches within the initiative. For example, the blinded processing of samples was not always ensured nor self-evident. The initiative did revisit and promoted blinding later on. Information gathered trough the initiative is shared in the European Network on Taeniosis/Cysticercosis, which allows learning at higher levels beyond this initiative. Although a high degree of organisational learning did take place, a change of fundamentals and objectives across all levels within the initiative did not explicitly take place. This is also not possible nor desirable within the design of the project. As this is a criterion of the NEOH framework, it incorrectly lowered the score for ‘adaptive and generative organisational learning’ to 0,63.

The stakeholders within CYSTISTOP were highly encouraging towards improving existing procedures and learning that focused on questioning the existing norms towards *T. solium* approaches. Therefore, ‘direct learning environment supportive of adaptive and generative learning’ received a perfect score (1) by all the interviewees.

The setting of the project did encourage the approach as the communities were supportive towards this initiative. Although, cultural groundings may present some limitations as behavioral changes might take a longer time to develop, which was stressed by some interviewees as some people were reported to still practice open defecation after a very intensive elimination program and education. Therefore, ‘general learning environment supportive of adaptive and generative learning’ scored 0,75.

The overall score obtained for OH learning is 0,78.

5.1.3.1.6 One Health infrastructure and systemic organisation

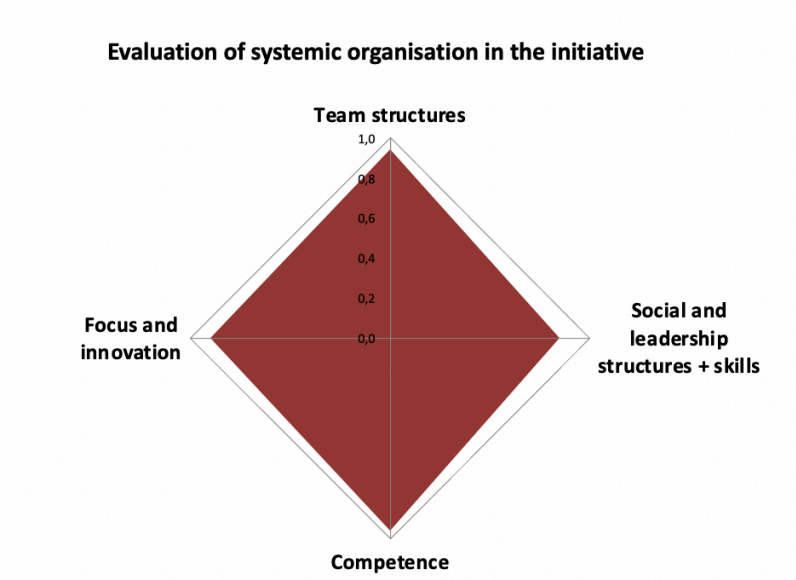

Figure 16. Spider diagram on the initiative's One Health systemic organisation processes. Obtained scores were: Team structures (0,94); Social and leadership structures + skills (0,85); competence (0,96); Focus and innovation (0,9).

The results obtained for OH infrastructure and systemic organisation are demonstrated in Figure 16. Teams were well structured and were clearly defined. As the initiative consisted out of several teams, it was highly based on teamwork that reported to be well-functioning. No competition between the teams and disciplines was reported by the interviewees. Inter-team relations were reported as good with all team members having clear objectives and very clearly differentiated roles for each team member within the team. Before each intervention, training was giving before the start by the head coordinator to ensure that each team and team members knew exactly what their roles, aims and objectives were as well as those of the other teams. Interviewees reported that the teams reflected after every intervention to assess their progress and to discuss their different opinions and outcomes. For example, some farmers experienced reluctance to needle use. Subsequently, the stakeholders took this feedback into account. Although changing needle use in this program would not be feasible, the initiative considered that in future interventions oral therapy might be better accepted. This also reflects a high degree of learning and open mindedness. Based on these results, a score of 0,94 is obtained for 'team structures'. Leadership within the initiative was not defined as relying on a single leader. Although a head coordinator was appointed, decision-making always occurred jointly and after approval of all involved disciplines. As a result, leadership was very balanced with the ability to manage occurring tensions, although none had been reported. In addition, a high level of open mindedness had been reported. These results translate into a score of 0,85 for 'social leadership and skill'.

Interdisciplinary competence fully responded to the aims and objectives of CYSTISTOP and therefore obtained a score of 0,96. 'Focus and innovation' scored 0,9 as the initiative was set up to be innovative with clear considerations of current knowledge and a clear formulation of gaps in research, opening to new opportunities to devise sustainable solutions. This can be illustrated by the fact that further research was carried out beyond the original objectives as certain pigs received a GPS tracker to track their roaming behaviour near the end of the study.

The overall score obtained for OH systemic organisation is 0,96.

5.1.3.1.7 The One Health Index and One Health Ratio

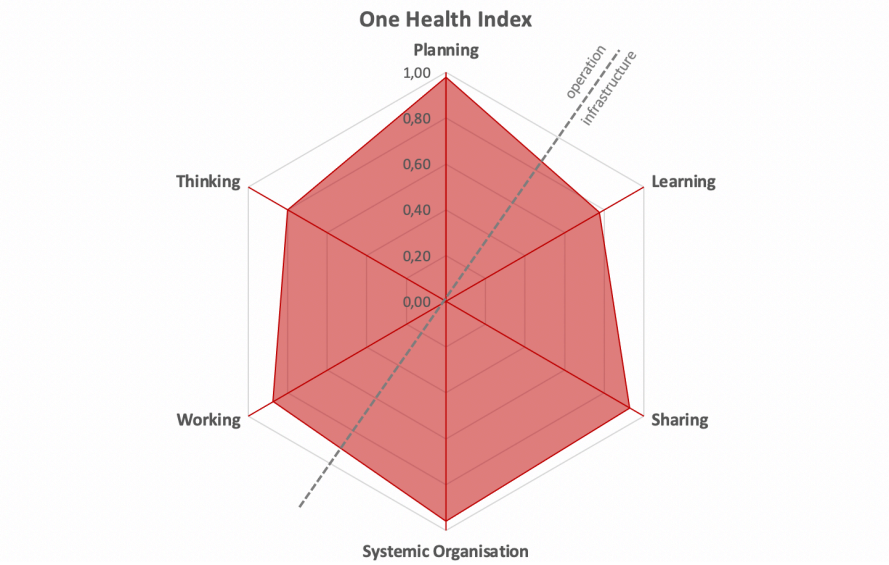

Figure 17. The One Health Index and One Health Ratio represented by the operational aspects ('thinking', 'planning' and 'working') and infrastructural aspects ('learning', 'sharing' and 'systemic organisation').

The results obtained for the OHI and OHR are demonstrated in Figure 17. The OHI, calculated as the proportion of the hexagon that is covered according to the individual scores obtained for each assessment tool, is 0,78. The OHR, the balance between the operational aspects and the infrastructural aspects, is 0,97.

5.1.4 Element 4: Assessment of the association(s) between the process evaluation and the outcomes produced

Due to delays associated with COVID 19, not all results are already available. Elimination was assessed and both control and the cost effectiveness of this study will be assessed in the coming months.

Available results on the prevalence of active porcine cysticercosis indicated a decrease from 32% at baseline to 0% in the intervention groups and from 32% to 25% in de control groups at the end of the elimination part of the study. These results emphasize that there is a significantly higher reduction of active porcine cysticercosis in the intervention group compared to the control group. A reduction from 16% to 2% in the intervention groups was additionally measured for the prevalence of taeniosis (Mwape et al., 2020).

Preliminary results on the sociological evaluation are already available and it appeared that the interventions are generally accepted by the community. Moreover, many respondents report to be willing to pay for medication. This is a positive outcome as it can contribute to future and larger-scale intervention programs implemented by the government (Hobbs et al., 2020).

For instance, some people from the elimination and control study community reported preliminary concerns and distrust about the request for blood and stool samples. Initially, these people were mainly concerned that the intervention program was satanic, or that collected blood would be sold by CYSTISTOP for economic profit, and concerns were additionally raised because people did not understand the process of the interventions. Later focus group discussions indicated that these people became increasingly confident in the project once they received education and could therefore better understand why certain interventions and blood tests were necessary (Hobbs et al., 2020).

Feedback from focus group discussions showed that there was a significant increase of latrine use, hand washing, and meat inspection since the start of education. In addition, people were more willing and aware about the added value to burry faeces according to the ‘cat method’ to prevent scavenging pigs to come in contact with human faeces (Hobbs et al., 2020). Although education increased awareness and led to some behavioural changes, it could not bring change in all practices. For example, it has been found that confining pigs is only poorly feasible by these communities in rural circumstances due to feed shortage. Another reason mentioned is that confined pigs appear to be more likely to be targeted by pig thieves. In addition, at the end of the intensive elimination program, people were still reported to practice open defecation (Hobbs et al., 2020).

A key finding by the researchers was that human-oriented interventions were much more accepted than pig-oriented interventions. As example, due to the outbreak of ASF in the study area, limitations did occur. There were heavy pig losses, an average of 600 pigs in each study area, in mid-2015. The participants in the study did agree in focus group discussions that these massive amounts of animals deceasing were due to ASF. However, in certain participants there was a suspicion that this was related to the interventions of the CYSTISTOP project mainly associated with vaccination through hypodermal injections, and less via oral treatments. This phenomenon became apparent as several pig-owners refused vaccination or even turned out to hide their animals from the intervention team (Hobbs et al., 2020).

6. Discussion

The results of this OH evaluation using the NEOH evaluation framework showed that the average of all six assessment tools was well above 0,80 (OH learning as an exception), directly impacting the OHI, that would be intuitively also scored as high. However, the assessment tools are plotted on the spokes of a spider diagram and the OHI is calculated as the proportion of the hexagon covered in comparison with a full coverage when all assessments would be scored 1, which translates in a lower score. Nevertheless, the obtained OHI indicates a high degree of OH integration. The obtained score for the OHR represents a high balance between infrastructure and organisational aspects, as the OHR is calculated as the symmetry between those aspects.

Indeed, CYSTISTOP responded well to the principles of OH. The implementation of a multidisciplinary approach was highly needed for CYSTISTOP to achieve its goals. The results of CYSTISTOP discussed in element 4 also show that CYSTISTOP has been successful so far, reducing active porcine cysticercosis in the elimination study arm to 0%. In addition, for taeniosis, a significant reduction in infection could be obtained. These results emphasize CYSTISTOP's stated outcomes of integrated intervention methods being more effective in reducing human *T. solium* and porcine cysticercosis infections than single options.

The eagerness to learn and critical self-assessment demonstrated in element 3 certainly played a major role in the already booked successes of CYSTISTOP. A OH approach advocates integrated feedback and adjustments. For initiatives carried out in developing countries and rural areas, feedback perception and willingness of the community are very important, as these factors are decisive for finding sustainable solutions that will persist even after the intervention. As discussed in element 4, operating in SSA has proven to be difficult and placing a great emphasis on local acceptability has contributed enormously to CYSTISTOP's booked successes and towards sustainability in the longer term. This indicates that in future interventions acceptability and socio-cultural aspects must always be considered and is in fact very much needed. Addressing these aspects in CYSTISTOP contributed to OH and the 3 Pillars of Sustainability. As these results are not reproducible for every area in SSA, as every community is different, there will remain a large need for the characterization of socio-cultural factors on a larger scale.

Strengths of this project are 'OH working' as strong team play and joint decision-making between stakeholders and disciplines is central and has reported to be much appreciated. Moreover, 'OH sharing' and 'OH systemic organisation' were trumps within this project, especially team structures, competence and innovation were well developed. As methods and results obtained through this pilot study are reported to be implemented in other studies, CYSTISTOP certainly achieved the goal of providing more sustainable solutions for SSA. Furthermore, some stakeholders stated that they explicitly received benefits from CYSTISTOP as it enabled their personal growth regarding the implementation of such projects and field interventions.

As stated in the literature review on OH, the environmental sector is often underrepresented in the OH approach, which is also the case for CYSTISTOP. The initiative could certainly have profited from involving the environmental sector more explicitly and beyond education as the environment is key in *T. solium* transmission. However, the limited presence of the environmental component was sufficient for CYSTISTOP to achieve its objectives. Yet, to fit the broader context of OH and to find sustainable solutions on a larger and higher scale, the environmental component was certainly not enough emphasized. Furthermore, in order to find more sustainability on a larger scale, more emphasis should be placed on the environmental sector and more stakeholders from higher levels should be involved in future interventions.

Although a lot of importance was given to joint decision making, the veterinary discipline was more prominently represented in the design and final decision making than human medicine was. This finding needs to be nuanced as these veterinarians have been working in the human medicine sector for a long time as well. Yet to fully answer to a OH approach, stakeholders from the veterinary as well as the medical and environmental sector need to be involved in the design of the project as well as in decision

making. Although there was a lot of interaction during the field interventions as well as in between, formal meetings with all disciplines and stakeholders involved were not held that frequent. The project could have benefited more from formal meetings to ensure that all disciplines are heard regularly by default allowing for even greater collaboration and communication.

Obtained scores in this evaluation need to be placed in perspective. Although this framework is ought to fit several initiatives and guidance is provided by the NEOH, it is not self-evident to do so as some criteria and questions are very specific and difficult to assess, or they might not be as suitable for this initiative causing potential inaccuracy in scoring. This finding has also been cited by other studies that have used the NEOH framework e.g. the study 'a One Health evaluation study regarding Brucellosis in Malta and Serbia conducted' by Buttigieg et al. This study additionally emphasizes the fact that since the NEOH evaluation framework is a relatively novel approach to evaluate OH, it is ideally complemented with other studies such as a cost-benefit analysis or cost effective analysis (Buttigieg et al., 2018). These studies contribute to OH as it facilitates different disciplines to work together and it provides evidence on benefits of intervention to authorities and enables funding (Baum et al., 2017). As COVID delayed this project, final results on cost-effectiveness are not fully available yet. These results on cost-effectiveness would have been very valuable to place CYSTISTOP's outcomes into perspective. Lack of complete results on all objectives is a limitation of this study as a full evaluation based on all the produced outcomes cannot be made.

Several studies are published in which the evaluation framework was used to assess the implementation of OH e.g. the comparison of 2 brucellosis intervention studies (Buttigieg et al., 2018), a study on obesity of dogs (Muñoz-Prieto et al., 2018), a cysticercosis surveillance system in Portugal (Fonseca et al., 2018) and the evaluation of OH within the University of Copenhagen Research for Control of Antibiotic Resistance (Léger et al., 2018). As the NEOH framework was published in 2018 and the studies being evaluated are very diverse, it is difficult to draw conclusions about the obtained results in comparison to other studies. Each study is context specific, and comparison is therefore hardly feasible. However, if this evaluation would be more systematically conducted and results would be collected and stored, comparison would be enabled in the future.

Traveling to Zambia to conduct this study would certainly have contributed to evaluate the initiative in an objective way without having to rely largely on the opinions of 'insiders' of CYSTISTOP. Although their opinions are very valuable, stakeholders may be biased, causing the answers given in the questionnaires to be not fully representative for the actual functioning of the project. In addition, these questionnaires were all addressed to high level stakeholders regarding implementation of CYSTISTOP. Including perspectives on actor level (nurses, local doctors and veterinarians) and community level would have provided additional valuable information. In addition, stakeholders interviewed element 3 of this study were either veterinarians or physicians, so no environmentalists or social scientists were involved despite their opinions being valuable in this multidisciplinary approach.

7. Conclusion

This research demonstrated that the integration of different disciplines was essential for *T. solium* research in SSA. This intervention study has been innovative and revolutionary in SSA conditions and CYSTISTOP did pave the way as obtained data and methods are already used in other studies. Ideally the environmental sector needs to be emphasized more in future interventions. Although, the evaluation framework proposed by the NEOH has certain limitations, it does stress the strengths and weaknesses of this project and provides a massive step forward to standardize OH evaluations.

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Appendix I. Interview and questionnaire protocol

A standardized protocol was implemented to conduct the study:

- Contact stakeholders via email, explain the thesis objectives and ask for willingness to participate
- Set a date
- Tools needed to conduct the study:
  List of people to contact
  Computer + charger
  Headphones
  Printed questionnaire
  Pen and paper to write down remarks
  Stable Wi-Fi connection or hotspot when needed
- Videocall via tele-conference held in English
  Start with introducing myself, explaining the objectives of the study
  Ask for oral agreement to use the data in this thesis and to record the interview
  Beginning the questionnaire
  Provide information when certain questions are unclear
  Finish questionnaire and thank participant
- Save answers on paper and in Google forms

Appendix II. Questionnaire

Underlined questions were excluded from the non-core group questionnaire.

Questionnaire CYSTISTOP

Thank you for participating in this study concerning my master's thesis assessing the CYSTISTOP project in the context of One Health.

The aim of this study is to evaluate the OH-ness of the CYSTISTOP and uncover the strengths and weaknesses following the principles of One Health (OH). The evaluation will be carried out using the framework developed and proposed by the Network for Evaluation of One Health (NEOH). The evaluation includes a questionnaire to be addressed to stakeholders involved in the project. The questionnaire addresses the OH principles that according to NEOH can be referred to as a multidisciplinary coordination, collaboration and communication between sectors with regard to the aspects of thinking, planning, working, sharing, learning and systemic organisation. The insights resulting from this evaluation may uncover the strengths and weaknesses of CYSTISTOP and provide useful information to the design and implementation of future projects and studies. If desired, the outcomes of this study will be shared with you.

One Health thinking

1. Rate the following statement:
   The initiative took a possible delay of work into consideration beforehand.
   a) Strongly agree
   b) Agree
   c) Undecided/neutral
   d) Disagree
   e) Strongly disagree
   f) I don't know

One Health planning

2. Was a planned organization (in terms of staff positions, involvement, participating institutions, networks, communication pathways, leadership etc.) of the initiative necessary and relevant to achieve the stated aims of the CYSTISTOP project? How would you consider the planning of the organization in terms of supportiveness towards a OH strategy?
   a) Organization fully supportive of a OH approach
   b) Organization highly supportive of a OH approach
   c) Organization supportive of a OH approach
   d) Organization somewhat supportive of a OH approach
   e) Organization slightly supportive of a OH approach
   f) Organization not supportive of a OH approach
   g) I don't know

3. Was essential stakeholder identification conducted in the planning of the initiative?
   a) All the stakeholders were identified perfectly
   b) High relevant identification process used
   c) Reasonable identification process used
   d) Identification process partly used
   e) Minor stakeholder identification was conducted

f) No stakeholder identification was conducted in the planning
g) I don't know

4. Was actor (e.g. Veterinarians, doctors, rural health centers) identification been described and followed in the planning of the initiative?
    a) All the actors were identified perfectly
    b) High relevant identification process used
    c) Reasonable identification process used
    d) Identification process partly used
    e) Minor actor identification was conducted
    f) No actor identification was conducted in the planning
    g) I don't know

5. Was the involvement and input of the different actors and stakeholders which were involved in the initiative taken into account in the planning of the initiative? How was the stakeholder engagement planned to ensure a OH approach in the working and organization stages of the initiative aiming to achieve the stated objectives and OH outcomes? Was there a mechanism to provide feedback from actors/stakeholders and to change methods within the initiative if required?
    a) Very strong stakeholder engagement, e.g. participation in planning and adjustments throughout the initiative
    b) High level of stakeholder engagement, e.g. participation in planning
    c) Reasonable stakeholder engagement, e.g. participation in implementation
    d) Some stakeholder engagement, e.g. workshops
    e) Little stakeholder engagement, e.g. questionnaires
    f) No stakeholder engagement, no feedback
    g) I don't know

6. Rate the following statement:
   The initiative allowed for 'underway'- corrections in planned activities or organizational aspects when needed.
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

7. Was time allocated for self-assessment in the initiative? Rate this statement from 0 to 5 with 0 no time was allocated and 5; time was allocated and accordingly used for self- assessment.

8. Was budget allocated for self-assessment in the initiative? Rate this statement from 0 to 5 with 0 no budget was allocated and 5; the budget was allocated and accordingly used for self-assessment.

One Health working

9. Were meetings with all disciplines (face to face or virtual) held frequently?
   Rate this question from 0-5 with 0: no frequently meetings involving all disciplines were held, and 5 meetings with all disciplines were held frequently.
   0-5

10. Were the aims and objectives shared and clear to all? Rate this question from 0 to 5 with 0: not clear and 5 clear to everyone.
    0-5

11. Was there joint decision making between the disciplines? Rate this question from 0 to 5 with 0: no joint decision making and 5 the initiative relied exclusively on joint decision making.
    0-5

12. How would you score the interaction between people within the initiative?
    a) Spontaneous frequent in person meetings
    b) Monthly planned in person meetings
    c) Quarterly meetings/skype meetings
    d) Little or rare interaction
    e) no interaction/collaboration
    f) I don't know

13. Which of these statements about the participating disciplines suits the CYSTISTOP initiative best?
    a) All disciplines were equally involved
    b) A few disciplines were slightly more influential than others
    c) Some disciplines were clearly more dominant than others
    d) One discipline took over
    e) I don't know

14. Which of these statements about the participating sectors suits the CYSTISTOP initiative best?
    a) All sectors were equally involved
    b) A few sectors were slightly more influential than others
    c) Some sectors were clearly more dominant than others
    d) One sector took over
    e) I don't know

15. Which of these statements about the participant's ethnicities suits the CYSTISTOP initiative the best?
    a) There was no imbalance between different ethnicities
    b) Some ethnicities were slightly favored in function
    c) One or more ethnicities were clearly disadvantaged
    d) I don't know

16. Which of these statements about the participant's social class suits the CYSTISTOP initiative best?
    a) There was no imbalance between different social classes
    b) Some social classes were slightly favored in function
    c) One or more social classes were clearly disadvantaged
    d) I don't know

17. Which of these statements about the gender of the participants suits the CYSTISTOP initiative best?
    a) There was no imbalance between gender
    b) One gender was slightly favored in function
    c) One gender took over
    d) I don't know

18. Which of these statements about cultural issues suits the CYSTISTOP initiative best?
    a) There were no cultural issues
    b) One culture was slightly favored in function

c) There was a disadvantage based on culture
d) I don't know

19. Which of these statements about religious issues between participants suits the CYSTISTOP initiative best?
    a) There were no religious issues
    b) One religion was slightly favored in function
    c) There was a disadvantage based on religion
    d) I don't know

20. How did CYSTISTOP deal with feedback and related adjustments?
    a) There was feedback and defined action pathway
    b) There was feedback without action
    c) There was no feedback
    d) I don't know

21. Rate the following statement:
    The project design was flexible to respond to internal or external changes at short term.
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

22. Rate the following statement:
    The project design was flexible to respond to internal or external changes at mid-term.
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

23. Rate the following statement:
    The project design was flexible to respond to internal or external changes at long-term.
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

One Health sharing

24. Did the initiative provide appropriate internal mechanisms to facilitate sharing of information within the initiative and were these used (e.g. newsletters, workshops, reports available for all, results getting published, online information sharing platform)?
    a) Yes, these were present and were intensively being used
    b) These were present and were used on a regularly basis
    c) These were present but only used when necessary
    d) These were present but not used
    g) These were not present
    h) I don't know

25. Did the initiative provide appropriate external mechanisms to facilitate sharing information outside of the initiative and where these used? (e.g. newsletters, workshops, reports available for all, results getting published, online information sharing platform)
    a) Yes, these were present and were intensively being used
    b) These were present and were used on a regularly basis
    c) These were present but only used when necessary
    d) These were present but not used
    e) These were not present
    f) I don't know

26. Rate the following statement:
    Resources were allocated to facilitate and ensure necessary data and information sharing within the initiative.
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

27. Rate the following statement:
    Mechanisms and procedures were taken into place to ensure data quality and allow sharing (e.g. data completeness, error-checking and correction of errors, clear and accurate descriptions of variables and of aggregations/calculations, documentation available).
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

28. Rate the following statement:
    Mechanisms/procedures were taken into place to ensure safe and appropriate data storage (type of software, server, backup) with safe accessibility to facilitate sharing (e.g. is extraction of data feasible without access of data managers, or are expert managers readily available for extraction of data, is the process of data extraction bureaucratic/cumbersome/overly time-consuming).
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

29. Were appropriate agreements made concerning data sharing in the initiative (e.g. how well and much data were being shared between people in the initiative)?
    a) Data was fully shared
    b) Data was shared between a few groups
    c) Compartmentalized sharing
    d) I don't know

30. How were methods shared between people within the initiative?
    a) Fully shared between all in the initiative
    b) Shared between a few groups in the initiative

c) Compartmentalized
d) I don't know

31. How were results shared between people within the initiative?
    a) Fully shared between all in the initiative
    b) Shared between a few groups in the initiative
    c) Compartmentalized
    d) I don't know

32. Rate the following statement:
    The initiative included the creation or use of potential institutional knowledge reservoirs for data, methods and/or results over time (e.g. publications, detailed reports/manuals, database descriptions, standard operating procedures, introductions to inform new staff on essential procedures)?
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

33. Rate the following statement:
    Mechanisms/procedures were in place to safe-guard access to data, information and results in case of system change, e.g. change of IT-system, data ownership, institutional organisations.
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

One Health learning

34. Was information you received through the initiative put into practice outside the initiative's context. (daily life, other projects).
    a) Always
    b) Very often
    c) Sometimes
    d) Rarely
    e) Never
    f) I don't know

35. Were your underlying beliefs and assumptions of knowledge and skill affected by the information provided by the initiative?
    a) Always
    b) Very often
    c) Sometimes
    d) Rarely
    e) Never
    f) I don't know

36. Information received through the initiative led to changing your underlying beliefs and norms affecting procedures, competencies and technologies in a beneficial way.

a) Always
b) Very often
c) Sometimes
d) Rarely
e) Never
f) I don't know

37. Teams (e.g. veterinary intervention team, or questionnaire team) had meetings to exchange information for reporting purposes.
    a) Always
    b) Very often
    c) Sometimes
    d) Rarely
    i) Never
    j) I don't know

38. During team meetings, different views were presented, defended and discussed to make sure to find the best view supporting decision making.
    a) Always
    b) Very often
    c) Sometimes
    d) Rarely
    e) Never
    f) I don't know

39. During team meetings complex issues were explored through dissection of views and assumptions of team members which led to creating new ideas, views or approaches.
    a) Always
    b) Very often
    c) Sometimes
    d) Rarely
    e) Never
    f) I don't know

40. Was existing information and knowledge about the context of the initiative (*T. solium*) collected and stored within the organization?
    a) Always
    b) Very often
    c) Sometimes
    d) Rarely
    e) Never
    f) I don't know

41. Was collected information shared and discussed and anticipated on at various levels within the organization?
    a) Always
    b) Very often
    c) Sometimes
    d) Rarely
    e) Never
    f) I don't know

42. Did sharing and discussing information lead to changes in fundamentals and objectives across all levels within the organization?
    a) Always

b) Very often
c) Sometimes
d) Rarely
e) Never
f) I don't know

43. Was the CYSTISTOP project encouraging the correction or improvement of existing procedures, processes, competences and technologies?
    a) Always
    b) Very often
    c) Sometimes
    d) Rarely
    e) Never
    f) I don't know

44. Was the CYSTISTOP project encouraging towards questioning the existing norms/situations?
    a) Always
    b) Very often
    c) Sometimes
    d) Rarely
    e) Never
    f) I don't know

45. Was the setting of the CYSTISTOP project encouraging towards correcting or improving existing procedures, processes, competences and technologies?
    a) Always
    b) Very often
    c) Sometimes
    d) Rarely
    e) Never
    f) I don't know

46. Was the setting of the CYSTISTOP project encouraging towards questioning the existing norms and values?
    a) Always
    b) Very often
    c) Sometimes
    d) Rarely
    e) Never
    f) I don't know

One Health systemic organisation

47. Rate the following statement:
    The different teams collaborated and worked well together leaving no room for competition.
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

48. Rate the following statement:
    All the teams had clear objectives

a) Strongly agree
b) Agree
c) Undecided/neutral
d) Disagree
e) Strongly disagree
f) I don't know

49. Rate from 0 to 5 how clearly the roles were differentiated for team members within the team with 5 a clear role differentiation and 0 no clarity about roles.
    0 - 5

50. Rate the following statement:
    The teams were recognized by the official organization as clearly defined teams.
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

51. How frequently did the teams meet to discuss their effectiveness and how the effectiveness could be improved?
    a) Frequently
    b) Very often
    c) Sometimes
    d) Rarely
    e) Never
    f) I don't know

52. Rate the following statement from 0 to 5 with 0 self-centered atmosphere and 5 a strong extroverted open-minded initiative.
    The initiative is considered as open minded, e.g. open to new suggestions and arguments, methods used in other disciplines and changes to the organisation that may improve impact.

53. Rate the following statement:
    The initiative could handle and manage occurring tensions.
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know

54. Rate the following statement:
    Multidisciplinary composition and competence in the teams permitted working towards the essential aspects of their objectives.
    a) Strongly agree
    b) Agree
    c) Undecided/neutral
    d) Disagree
    e) Strongly disagree
    f) I don't know